PCT

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(51) International Patent Classification 5:		(11) International Publication Number: WO 94/2560
C12N 15/51, C12Q 1/68, A61K 39/29, G01N 33/576, C07N 14/18, C12Q 1/70, C07K 16/10	A2	(43) International Publication Date: 10 November 1994 (10.11.94
934(20)19.9 '5 August 1959 (10.508.93) (34) Countries for which the regional or international application was filed: (71) Applicant (for all designated States except US): N.V. GENETICS S.A. (BE/BE]: Industriepark, Zwihni BOX 4, B-9052 Ghent (BE). (72) Laventors/applicants (for US only): MAERTENS (BE/BE]: Zilversparenstrasse 64, B-8310 Brugg (BE/BE]: Zilversparenstrasse 64, B-8310 Brugg	EB et a EB et a INNO sarde	CZ, DE, DK, ES, FI, CB, GE, HU, IP, KG, KP, KI KZ, KZ, LJ, LI, V, MD, MG, MN, MW, NI, NO, NZ, PI PT, RO, RU, SD, SE, SI, SK, TI, TT, UA, US, UZ, VI European patent (AT, BE, CH, DE, DK, ES, FR, GB, GP, IE, TT, LU, MC, NI, PT, SB, OAPI patent (BF, BJ, CI CC, CL, CM, GA, CN, ML, MR, NE, SN, TD, TG) Published Without international search report and to be republished upon receipt of that report.
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(57) Abstract

The present invention relates to a polynucleic acid composition comprising or consisting of at least one polynucleic acid containing or more contiguous nucleotides corresponding to a nucleotide sequence from the region spanning positions 417 to 957 of the Correllar region of HCV type 3; and/or the region spanning positions 4692 to 7500 of the NS3 region of HCV type 3; and/or the region spanning positions 4892 to 5292 of the NS34 region of HCV type 8; and/or the region spanning positions 4802 to 8230 to 8235 of the NS34 region of HCV type 4; and/or the region admost the region spanning positions 4802 to 7502 of the NS34 region of HCV type 4; and/or the region admost the region of HCV type 4; and/or the region of HCV t type 1, and/or HCV type 2 genomes in the above-indicated regions, or the complement thereof.



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NEW SEQUENCES OF HEPATITIS C VIRUS GENOTYPES AND THEIR USE AS THERAPEUTIC AND DIAGNOSTIC AGENTS

The invention relates to new sequences of hepatitis C virus (HCV) genotypes and their use as therapeutic and diagnostic agents.

The present invention relates to new nucleotide and amino acid sequences corresponding to the coding region of a new type 2 subtype 2d, type-specific sequences corresponding to HCV type 3a, to new sequences corresponding to the coding region of a new subtype 3c, and to new sequences corresponding to the coding region of HCV type 4 and type 5 subtype 5a; a process for preparing them, and their use for diagnosis, prophylaxis and therapy.

The technical problem underlying the present invention is to provide new type-specific sequences of the Core, the E1, the E2, the NS3, the NS4 and the NS5 regions of HCV type 4 and type 5, as well as of new variants of HCV types 2 and 3. These new HCV sequences are useful to diagnose the presence of type 2 and/or type 3 and/or type 4 and/or type 5 HCV genotypes in a biological sample. Moreover, the availability of these new type-specific sequences can increase the overall sensitivity of HCV detection and should also prove to be useful for therapeutic purposes.

Hepatitis C viruses (HCV) have been found to be the major cause of non-A, non-B hepatitis. The sequences of cDNA clones covering the complete genome of several prototype isolates have been determined (Kato et al., 1990; Choo et al., 1991; Okamoto et al., 1992). Comparison of these isolates shows that the variability in nucleotide sequences can be used to distinguish at least 2 different genotypes, type 1 (HcV-1 and HCV-1) and type 2 (HC-16 and HC-18), with an average homology of about 68%. Within each type, at least two subtypes exist (e.g. represented by HCV-1 and HCV-J), having an average homology of about 79%. HCV genomes belonging to the same subtype show average homologies of more than 90% (Okamoto et al., 1992). However, the partial nucleotide sequence of the NS5 region of the HCV-T isolates showed at most 67% homology with the previously published sequences, indicating the existence of a yet another HCV type (Mori et al., 1992). Parts of the 5' untranslated region (UR), core, NS3, and NS5 regions of this type 3 have been published, further establishing the similar evolutionary distances between the 3 major genotypes and their subtypes (Chan et al., 1992).

The identification of type 3 genotypes in clinical samples can be achieved by means of PCR with type-specific primers for the NS5 region. However, the degree to which this will be successful is largely dependent on sequence variability and on the virus titer present in the serum. Therefore, routine PCR in the open reading frame, especially for type 3 and the new type 4 and 5 described in the present invention and/or group V (Cha et al., 1992) genotypes can be predicted to be unsuccessful. A new typing system (LiPA), based on variation in the highly conserved 5' UR, proved to be more useful because the 5 major HCV genotypes and their subtypes can be determined (Stuyver et al., 1993). The selection of high-titer isolates enables to obtain PCR fragments for cloning with only 2 primers, while nested PCR requires that 4 primers match the unknown sequences of the new type 3, 4 and 5 genotypes.

New sequences of the 5' untranslated region (5'UR) have been listed by Bukh et al. (1992). For some of these, the E1 region has recently been described (Bukh et al., 1993). Isolates with similar sequences in the 5'UR to a group of isolates including DK12 and HK10 described by Bukh et al. (1992) and E-b1 to E-b8 described and classified as type 3 by Chan et al. (1991), have been reported and described in the 5'UR, the carboxyterminal part of E1, and in the NS5 region as group IV by Cha et al. (1992; WO 92/19743), and have also been described in the 5'UR for isolate BR56 and classified as type 3 by the inventors of this application (Stuyver et al., 1993).

The aim of the present invention is to provide new HCV nucleotide and amino acid sequences enabling the detection of HCV infection.

Another aim of the present infection is to provide new nucleotide and amino acid HCV sequences enabling the classification of infected biological fluids into different serological groups unambiguously linked to types and subtypes at the genome level.

Another aim of the present invention is to provide new nucleotide and amino acid HCV sequences ameliorating the overall HCV detection rate.

Another aim of the present invention is to provide new HCV sequences, useful for the design of HCV vaccine compositions.

Another aim of the present invention is to provide a pharmaceutical composition consisting of antibodies raised against the polypeptides encoded by these new HCV sequences, for therapy or diagnosis.

The present invention relates more particularly to a composition comprising or consisting of at least one polynucleic acid containing at least 5, and preferably 8 or more contiguous nucleotides selected from at least one of the following HCV sequences:

 an HCV type 3 genomic sequence, more particularly in any of the following regions:

- the region spanning positions 417 to 957 of the Core/E1 region of HCV subtype 3a,
- the region spanning positions 4664 to 4730 of the NS3 region of HCV type
 3,
- the region spanning positions 4892 to 5292 of the NS3/4 region of HCV type 3,
- the region spanning positions 8023 to 8235 of the NS5 region of the BR36 subgroup of HCV subtype 3a,
- an HCV subtype 3c genomic sequence,

more particularly the coding regions of the above-specified regions;

- an HCV subtype 2d genomic sequence, more particularly the coding region of HCV subtype 2d;
- an HCV type 4 genomic sequence, more particularly the coding region, more particularly the coding region of subtypes 4a, 4e, 4f, 4g, 4h, 4i, and 4j,
- an HCV type 5 genomic sequence, more particularly the coding region of HCV type 5, more particularly the regions encoding Core, E1, E2, NS3, and NS4

with said nucleotide numbering being with respect to the numbering of HCV nucleic acids as shown in Table 1, and with said polynucleic acids containing at least one nucleotide difference with known HCV (type 1, type 2, and type 3) polynucleic acid sequences in the above-indicated regions, or the complement thereof.

It is to be noted that the nucleotide difference in the polynucleic acids of the invention may involve or not an amino acid difference in the corresponding amino acid sequences coded by said polynucleic acids.

According to a preferred embodiment, the present invention relates to a composition comprising or containing at least one polynucleic acid encoding an HCV polyprotein, with said polynucleic acid containing at least 5, preferably at least 8 nucleotides corresponding to at least part of an HCV nucleotide sequence encoding an HCV polyprotein, and with said HCV polyprotein containing in its sequence at least one of the following amino acid residues: L7, Q43, M44, S60, R67, Q70, T71, A79, A87, N106, K115, A127, A190, S130, V134, G142, I144, E152, A157, V158, P165, S177 or Y177, I178, V180 or E180 or F182, R184, I186, H187, T189, A190, S191 or G191, Q192 or L192 or I192 or V192 or E192, N193 or H193 or P193, W194 or Y194, H195, A197 or I197 or V197 or T197, V202, I203 or L203, Q208, A210, V212, F214, T216, R217 or D217 or E217 or V217, H218 or N218, H219 or

V219 or L219, L227 or I227, M231 or E231 or Q231, T232 or D232 or A232 or K232, Q235 or I235, A237 or T237, I242, I246, S247, S248, V249, S250 or Y250, I251 or V251 or M251 or F251, D252, T254 or V254, L255 or V255, E256 or A256, M258 or F258 or V258, A260 or Q260 or S260, A261, T264 or Y264, M265, I266 or A266, A267, G268 or T268. F271 or M271 or V271. I277, M280 or H280. I284 or A284 or L84, V274, V291. N292 or S292, R293 or I293 or Y293, Q294 or R294, L297 or I297 or Q297, A299 or K299 or Q299, N303 or T303, T308 or L308, T310 or F310 or A310 or D310 or V310, L313, G317 or Q317, L333, S351, A358, A359, A363, S364, A366, T369, L373, F376, Q386, I387, S392, I399, F402, I403, R405, D454, A461, A463, T464, K484, Q500, E501, S521, K522, H524, N528, S531, S532, V534, F536, F537, M539, I546, C1282, A1283, H1310, V1312, Q1321, P1368, V1372, V1373, K1405, Q1406, S1409, A1424, A1429, C1435. S1436, S1456, H1496, A1504, D1510, D1529, I1543, N1567, D1556, N1567, M1572, Q1579, L1581, S1583, F1585, V1595, E1606 or T1606, M1611, V1612 or L1612, P1630, C1636, P1651, T1656 or I1656, L1663, V1667, V1677, A1681, H1685, E1687, G1689, V1695, A1700, Q1704, Y1705, A1713, A1714 or S1714, M1718, D1719, A1721 or T1721, R1722, A1723 or V1723, H1726 or G1726, E1730, V1732, F1735, I1736, S1737, R1738, T1739, G1740, Q1741, K1742, Q1743, A1744, T1745, L1746, E1747 or K1747, I1749, A1750, T1751 or A1751, V1753, N1755, K1756, A1757, P1758, A1759, H1762, T1763, Y1764, P2645, A2647, K2650, K2653 or L2653, S2664, N2673, F2680, K2681, L2686, H2692, Q2695 or L2695 or I2695, V2712, F2715, V2719 or Q2719, T2722, T2724, S2725. R2726, G2729, Y2735, H2739, I2748, G2746 or I2746, I2748, P2752 or K2752, P2754 or T2754. T2757 or P2757, with said notation being composed of a letter representing the amino acid residue by its one-letter code, and a number representing the amino acid numbering according to Kato et al., 1990.

Each of the above-mentioned residues can be found in any of Figures 2, 5, 7, 11 or 12 showing the new amino acid sequences of the present invention aligned with known sequences of other types or subtypes of HCV for the Core, E1, E2, NS3, NS4, and NS5 regions.

More particularly, a polynucleic acid contained in the composition according to the present invention contains at least 5, preferably 8, or more contiguous nucleotides corresponding to a sequence of contiguous nucleotides selected from at least one of HCV sequences encoding the following new HCV amino acid sequences:

 new sequences spanning amino acid positions 1 to 319 of the Core/E1 region of HCV subtype 2d, type 3 (more particularly new sequences for subtypes 3a and 3c), new type 4 WO 94/25601 PCT/EP94/01323

5 subtypes (more particularly new sequences for subtypes 4a, 4e, 4f, 4g, 4h, 4i and 4i) and type 5a, as shown in Figure 5:

- new sequences spanning amino acid positions 328 to 546 of the E1/E2 region of HCV subtype 5a as shown in Figure 12;
- new sequences spanning amino acid positions 1556 to 1764 of the NS3/NS4 region of HCV type 3 (more particularly for new subtypes 3a sequences), and subtype 5a, as shown in Figure 7 or 11;
- new sequences spanning amino acid positions 2645 to 2757 of the NS5B region of HCV subtype 2d, type 3 (more particularly for new subtypes 3a and 3c), new type 4 subtypes (more particularly subtypes 4a, 4e, 4f, 4g, 4h, 4i and 4i) and subtype 5a, as shown in Figure 2,

Using the LiPA system mentioned above, Brazilian blood donors with high titer type 3 hepatitis C virus, Gabonese patients with high-titer type 4 hepatitis C virus, and a Belgian patient with high-titer HCV type 5 infection were selected. Nucleotide sequences in the core, E1, NS5 and NS4 regions which have not yet been reported before, were analyzed in the frame of the invention. Coding sequences (with the exception of the core region) of any type 4 isolate are reported for the first time in the present invention. The NS5b region was also analyzed for the new type 3 isolates. After having determined the NS5b sequences. comparison with the Ta and Tb subtypes described by Mori et al. (1992) was possible, and the type 3 sequences could be identified as type 3a genotypes. The new type 4 isolates segregated into 10 subtypes, based on homologies obtained in the NS5 and E1 regions, New type 2 and 3 sequences could also be distinguished from previously described type 2 or 3 subtypes from sera collected in Belgium and the Netherlands.

The term "polynucleic acid" refers to a single stranded or double stranded nucleic acid sequence which may contain at least 5 contiguous nucleotides to the complete nucleotide sequence (f.i. at least 6, 7, 8, 9, 10, 11, 12, 13, 14, 15 or more contiguous nucleotides). A polynucleic acid which is up till about 100 nucleotides in length is often also referred to as an oligonucleotide. A polynucleic acid may consist of deoxyribonucleotides or ribonucleotides, nucleotide analogues or modified nucleotides, or may have been adapted for therapeutic purposes. A polynucleic acid may also comprise a double stranded cDNA clone which can be used for cloning purposes, or for in vivo therapy, or prophylaxis.

The term "polynucleic acid composition" refers to any kind of composition comprising essentially said polynucleic acids. Said composition may be of a diagnostic or a therapeutic

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nature.

The expression "nucleotides corresponding to" refers to nucleotides which are homologous or complementary to an indicated nucleotide sequence or region within a specific HCV sequence.

The term "coding region" corresponds to the region of the HCV genome that encodes the HCV polyprotein. In fact, it comprises the complete genome with the exception of the 5' untranslated region and 3' untranslated region.

The term "HCV polyprotein" refers to the HCV polyprotein of the HCV-J isolate (Kato et al., 1990). The adenine residue at position 330 (Kato et al., 1990) is the first residue of the ATG codon that initiates the long HCV polyprotein of 3010 amino acids in HCV-J and other type 1b isolates, and of 3011 amino acids in HCV-I and other type 1a isolates, and of 3033 amino acids in type 2 isolates HC-J6 and HC-J8 (Okamoto et al., 1992).

This adenine is designated as position 1 at the nucleic acid level, and this methionine is designated as position 1 at the amino acid level, in the present invention. As type 1a isolates contain 1 extra amino acid in the NS5a region, coding sequences of type 1a and 1b have identical numbering in the Core, E1, NS3, and NS4 region, but will differ in the NS5b region as indicated in Table 1. Type 2 isolates have 4 extra amino acids in the E2 region, and 17 or 18 extra amino acids in

the NS5 region compared to type 1 isolates, and will differ in numbering from type 1 isolates in the NS3/4 region and NS5b regions as indicated in Table 1.

TABLE 1

	Region	Positions described in the present invention*	Positions described for HCV-J (Kato et al., 1990)	Positions described for HCV-1 (Choo et al., 1991)	Positions described for HC-J6, HC-J8 (Okamoto et al., 1992)
Nucleotide s	NS5b	8023/8235 7932/8271	8352/8564 8261/8600	8026/8238 7935/8274	8433/8645 8342/8681
	NS3/4	4664/5292 4664/4730 4892/5292 3856/4209 4936/5292	4993/5621 4993/5059 5221/5621 4185/4528 5265/5621	4664/5292 4664/4730 4892/5292 3856/4209 4936/5292	5017/5645 5017/5083 5245/5645 4209/4762 5289/5645
		coding region of present invention	330/9359	1/9033	342/9439
Amino Acids	NS5b	2675/2745 2645/2757	2675/2745 2645/2757	2676/2746 2646/2758	2698/2768 2668/2780
	NS3/4	1556/1764 1286/1403 1646/1764	1556/1764 1286/1403 1646/1764	1556/1764 1286/1403 1646/1764	1560/1768 1290/1407 1650/1768

Table 1: Comparison of the HCV nucleotide and amino acid numbering system used in the present invention (*) with the numbering used for other prototype isolates. For example, 8352/8564 indicates the region designated by the numbering from nucleotide 8352 to nucleotide 8564 as described by Kato et al. (1990). Since the numbering system of the present invention starts at the polyprotein initiation site, the 329 nucleotides of the 5' untranslated region described by Kato et al. (1990) have to be substracted, and the corresponding region is numbered from nucleotide 8023 ("8352-329") to 8235 ("8564-329").

The term "HCV type" corresponds to a group of HCV isolates of which the complete genome shows more than 74% homology at the nucleic acid level, or of which the NS5 region between nucleotide positions 7932 and 8271 shows more than 74% homology at the nucleic acid level, or of which the complete HCV polyprotein shows more than 78% homology at the amino acid level, or of which the NS5 region between amino acids at positions 2645 and 2757 shows more than 80% homology at the amino acid level, to polyproteins of the other isolates of the group, with said numbering beginning at the first ATG codon or first methionine of the long HCV polyprotein of the HCV-J isolate (Kato et al., 1990). Isolates belonging to different types of HCV exhibit homologies, over the complete genome, of less than 74% at the nucleic acid level and less than 78% at the amino acid level. Isolates belonging to the same type usually show homologies of about 92 to 95% at the nucleic acid level and 95 to 96% at the amino acid level when belonging to the same subtype, and those belonging to the same type but different subtypes preferably show homologies of about 79% at the nucleic acid level and 85-86% at the amino acid level.

More preferably the definition of HCV types is concluded from the classification of HCV isolates according to their nucleotide distances calculated as detailed below:

- (1) based on phylogenetic analysis of nucleic acid sequences in the NS5b region between nucleotides 7935 and 8274 (Choo et al., 1991) or 8261 and 8600 (Kato et al., 1990) or 8342 and 8681 (Okamoto et al., 1991), isolates belonging to the same HCV type show nucleotide distances of less than 0.34, usually less than 0.33, and more usually of less than 0.135, usually of less than 0.131, and more usually of less than 0.125, and consequently isolates belonging to the same type but different subtypes show nucleotide distances ranging from 0.135 to 0.34, usually ranging from 0.1384 to 0.2477, and more usually ranging from 0.15 to 0.32, and isolates belonging to different HCV types show nucleotide distances greater than 0.34, usually greater than 0.35, and more usually of greater than 0.35, and more usually ranging from 0.1384 to 0.2977.
- (2) based on phylogenetic analysis of nucleic acid sequences in the core/E1 region between nucleotides 378 and 957, isolates belonging to the same HCV type show nucleotide distances of less than 0.38, usually of less than 0.37, and more usually of less than 0.364, and isolates belonging to the same subtype show nucleotide distances of less than 0.17, usually of less than 0.16, and more usually of less than 0.15, more usually less than 0.135, more usually less than 0.134, and consequently isolates belonging to the same type but different subtypes show

nucleotide distances ranging from 0.15 to 0.38, usually ranging from 0.16 to 0.37, and more usually ranging from 0.17 to 0.36, more usually ranging from 0.133 to 0.379, and isolates belonging to different HCV types show nucleotide distances greater than 0.34, 0.35, 0.36, usually more than 0.365, and more usually of greater than 0.37.

(3) based on phylogenetic analysis of nucleic acid sequences in the NS3/NS4 region between nucleotides 4664 and 5292 (Choo et al., 1991) or between nucleotides 4993 and 5621 (Kato et al., 1990) or between nucleotides 5017 and 5645 (Okamoto et al., 1991), isolates belonging to the same HCV type show nucleotide distances of less than 0.35, usually of less than 0.34, and more usually of less than 0.33, and isolates belonging to the same subtype show nucleotide distances of less than 0.19, usually of less than 0.18, and more usually of less than 0.17, and consequently isolates belonging to the same type but different subtypes show nucleotide distances ranging from 0.17 to 0.35, usually ranging from 0.18 to 0.34, and more usually ranging from 0.19 to 0.33, and isolates belonging to different HCV types show nucleotide distances greater than 0.33, usually greater than 0.34, and more usually of greater than 0.35.

Table 2 : Molecular evolutionary distances

Region	Core/E1	E1	NS5B	NS5B
	579 bp	384 bp	340 bp	222 bp
Isolates*	0.0017 - 0.1347	0.0026 - 0.2031	0.0003 - 0.1151	0.000 - 0.1323
	(0.0750 ± 0.0245)	(0.0969 <u>+</u> 0.0289)	(0.0637 <u>+</u> 0.0229)	(0.0607 <u>+</u> 0.0205)
Subtypes*	0.1330 - 0.3794	0.1645 - 0.4869	0.1384 - 0.2977	0.117 - 0.3538
	(0.2786 ± 0.0363)	(0.3761 <u>+</u> 0.0433)	(0.2219 ± 0.0341)	(0.2391 <u>+</u> 0.0399)
Types*	0.3479 - 0.6306	0.4309 - 0.9561	0.3581 - 0.6670	0.3457 - 0.7471
	(0.4703 <u>+</u> 0.0525)	(0.6308 ± 0.0928)	(0.4994 <u>+</u> 0.0495)	(0.5295 <u>+</u> 0.0627)

Figures created by the PHYLIP program DNADIST are expressed as minimum to maximum (average ± standard deviation). Phylogenetic distances for isolates belonging to the same subtype ('isolates'), to different subtypes of the same type ('subtypes'), and to different types ('types') are given.

In a comparative phylogenetic analysis of available sequences, ranges of molecular evolutionary distances for different regions of the genome were calculated, based on 19,781

pairwise comparisons by means of the DNA DIST program of the phylogeny inference package PHYLIP version 3.5C (Felsenstein, 1993). The results are shown in Table 2 and indicate that although the majority of distances obtained in each region fit with classification of a certain isolate, only the ranges obtained in the 340bp NS5B-region are non-overlapping and therefor conclusive. However, as was performed in the present invention, it is preferable to obtain sequence information from at least 2 regions before final classification of a given isolate.

Designation of a number to the different types of HCV and HCV types nomenclature is based on chronological discovery of the different types. The numbering system used in the present invention might still fluctuate according to international conventions or guidelines. For example, "type 4" might be changed into "type 5" or "type 6".

The term "subtype" corresponds to a group of HCV isolates of which the complete polyprotein shows a homology of more than 90% both at the nucleic acid and amino acid levels, or of which the NS5 region between nucleotide positions 7932 and 8271 shows a homology of more than 90% at the nucleic acid level to the corresponding parts of the genomes of the other isolates of the same group, with said numbering beginning with the adenine residue of the initiation codon of the HCV polyprotein. Isolates belonging to the same type but different subtypes of HCV show homologies of more than 74% at the nucleic acid level and of more than 78% at the amino acid level.

The term "BR36 subgroup" refers to a group of type 3a HCV isolates (BR36, BR33, BR34) that are 95 %, preferably 95.5 %, most preferably 96 % homologous to the sequences as represented in SEQ ID NO 1, 3, 5, 7, 9, 11 in the NS5b region from position 8023 to 8235.

It is to be understood that extremely variable regions like the E1, E2 and NS4 regions will exhibit lower homologies than the average homology of the complete genome of the polyprotein.

Using these criteria, HCV isolates can be classified into at least 6 types. Several subtypes can clearly be distinguished in types 1, 2, 3 and 4: 1a, 1b, 2a, 2b, 2c, 2d, 3a, 3b, 4a, 4b, 4c, 4d, 4e, 4f, 4g, 4h, 4i and 4j based on homologies of the 5' UR and coding regions including the part of NS5 between positions 7932 and 8271. An overview of most of the reported isolates and their proposed classification according to the typing system of the present invention as well as other proposed classifications is presented in Table 3.

Table 3

HCV CLASSIFICATION

	OKA- MOTO	MORI	NAKA O	СНА	РКОТОТУРЕ
la	I	I	Pt	GI	HCV-1, HCV-H, HC-J1
1b	П	п	KI	GII	HCV-J, HCV-BK, HCV-T, HC-JK1, HC- J4, HCV-CHINA
1c					HC-G9
2a	ш	ш	K2a	GIII	HC-J6
2b	IV	IV	K2b	GIII	HC-J8
2c					S83, ARG6, ARG8, I10, T983
2đ					NE92
-3a	v	v	K3	GIV	E-b1, Ta, BR36, BR33, HD10, NZL1
3b		VI	К3	GIV	HCV-TR, Tb
3c					BE98
4a					Z4, GB809-4
4b				-	Z1
4c					GB116, GB358, GB215, Z6, Z7
4d					DK13
4e					GB809-2, CAM600, CAM736
4f					CAM622, CAM627
4g					GB549 .
4h		9			GB438
4i					CAR4/1205
4j					CAR1/501
4k					EG29
5a				GV	SA3, SA4, SA1, SA7, SA11, BE95
6a					HK1, HK2, HK3, HK4

The term "complement" refers to a nucleotide sequence which is complementary to an indicated sequence and which is able to hybridize to the indicated sequences.

The composition of the invention can comprise many combinations. By way of example, the composition of the invention can comprise:

- two (or more) nucleic acids from the same region or,
- two nucleic acids (or more), respectively from different regions, for the same isolate or for different isolates,
- or nucleic acids from the same regions and from at least two different regions (for the same isolate or for different isolates).

The present invention relates more particularly to a polynucleic acid composition as defined above, wherein said polynucleic acid corresponds to a nucleotide sequence selected from any of the following HCV type 3 genomic sequences:

- an HCV genomic sequence having a homology of at least 67%, preferably more than 69%, more preferably 71%, even more preferably more than 73%, or most preferably more than 76% to any of the sequences as represented in SEQ ID NO 13, 15, 17, 19, 21, 23, 25 or 27 (HD10, BR36 or BR33 sequences) in the region spanning positions 417 to 957 of the Core/E1 region as shown in Figure 4;
- an HCV genomic sequence having a homology of at least 65%, preferably more than 67%, preferably more than 69%, even preferably more than 70%, most preferably more than 74% to any of the sequences as represented in SEQ ID NO 13, 15, 17, 19, 21, 23, 25 or 27 (HD10, BR36 or BR33 sequences) in the region spanning positions 574 to 957 of the E1 region as shown in Figure 4;
- an HCV genomic sequence as having a homology of at least 79%, more preferably at least 81%, most preferably more than 83% or more to any of the sequences as represented in SEQ ID NO 147 (representing positions 1 to 346 of the Core region of HVC type 3c, sequence BE98) in the region spanning positions 1 to 378 of the Core region as shown in Figure 3;
- an HCV genomic sequence of HVC type 3a having a homology of at least 74%, more preferably at least 76%, most preferably more than 78% or more to any of the sequences as represented in SEQ ID NO 13, 15, 17, 19, 21, 23, 25 or 27 (HD10, BR36 or BR33 sequences) in the region spanning positions 417 to 957 in the Core/E1 region as shown in Figure 4;
- an HCV genomic sequence of HCV type 3a as having a homology of at least 74%,

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preferably more than 76%, most preferably 78% or more to any of the sequences as represented in SEQ ID NO 13, 15, 17, 19, 21, 23, 25 or 27 (HD10, BR36 or BR33 sequences) in the region spanning positions 574 to 957 in the E1 region as shown in Figure 4:

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- an HCV genomic sequence as having a homology of more than 73.5%, preferably more than 74%, most preferably 75% homology to the sequence as represented in SEQ ID NO
 29 (HCCl53 sequence) in the region spanning positions 4664 to 4730 of the NS3 region as shown in figure 6;
- an HCV genomic sequence having a homology of more than 70%, preferably more than 72%, most preferably more than 74% homology to any of the sequences as represented in SEQ ID NO 29, 31, 33, 35, 37 or 39 (HCCl53, HD10, BR36 sequences) in the region spanning positions 4892 to 5292 in the NS3/NS4 region as shown in Figure 6 or 10:
- an HCV genomic sequence of the BR36 subgroup of HCV type 3a as having a homology of more than 95%, preferably 95,5%, most preferably 96% homology to any of the sequences as represented in SEQ ID NO 5, 7, 1, 3, 9 or 11 (BR34, BR33, BR36 sequences) in the region spanning positions 8023 to 8235 of the NS5 region as shown in Figure 1:
- an HCV genomic sequence of the BR36 subgroup of HCV type 3a as having a homology of more than 96%, preferably 96.5%, most preferably 97% homology to any of the sequences as represented in SEQ ID NO 5, 7, 1, 3, 9 or 11 (BR34, BR33, BR36 sequences) in the region spanning positions 8023 to 8192 of the NS5B region as shown in Figure 1;
- an HCV genomic sequence of HCV type 3c being characterized as having a homology of more than 79%, more preferably more than 81%, and most preferably more than 83% to the sequence as represented in SEQ ID NO 149 (BE98 sequence) in the region spanning positions 7932 to 8271 in the NS5B region as shown in Figure 1.

Preferentially the above-mentioned genomic HCV sequences depict sequences from the coding regions of all the above-mentioned sequences.

According to the nucleotide distance classification system (with said nucleotide distances being calculated as explained above), said sequences of said composition are selected from:

- an HCV genomic sequence being characterized as having a nucleotide distance of less than 0.44, preferably of less than 0.40, most preferably of less than 0.36 to any of the sequences as represented in SEO ID NO 13, 15, 17, 19, 21, 23, 25 or 27 in the region

- spanning positions 417 to 957 of the Core/E1 region as shown in Figure 4;
- an HCV genomic sequence being characterized having a nucleotide distance of less than 0.53, preferably less than 0.49, most preferably of less than 0.45 to any of the sequences as represented in SEQ ID NO 19, 21, 23, 25 or 27 in the region spanning positions 574 to 957 of the E1 region as shown in Figure 4;
- an HCV genomic sequence characterized having a nucleotide distance of less than 0.15, preferably less than 0.13, and most preferably less than 0.11 to any of the sequences as represented in SEQ ID NO 147 in the region spanning positions 1 to 378 of the Core region as shown in Figure 3;
- an HCV genomic sequence of HVC type 3a being characterized as having a nucleotide distance of less than 0.3, preferably less than 0.26, most preferably of less than 0.22 to any of the sequences as represented in SEQ ID NO 13, 15, 17, 19, 21, 23, 25 or 27 in the region spanning positions 417 to 957 in the Core/E1 region as shown in Figure 4;
- an HCV genomic sequence of HCV type 3a being characterized as having a nucleotide distance of less than 0.35, preferably less than 0.31, most preferably of less than 0.27 to any of the sequences as represented in SEQ ID NO 13, 15, 17, 19, 21, 23, 25 or 27 in the region spanning positions 574 to 957 in the E1 region as shown in Figure 4;
- an HCV genomic sequence of the BR36 subgroup of HCV type 3a being characterized as having a nucleotide sequence of less than 0.0423, preferably less than 0.042, preferably less than 0.0362 to any of the sequences as represented in SEQ ID NO 5, 7, 1, 3, 9 or 11 in the region spanning positions 8023 to 8235 of the NS5 region as shown in Figure 1:
- an HCV genomic sequence of HCV type 3c being characterized as having a nucleotide distance of less than 0.255, preferably of less than 0.25, more preferably of less than 0.21, most preferably of less than 0.17 to the sequence as represented in SEQ ID NO 149 in the region spanning positions 7932 to 8271 in the NS5B region as shown in Figure 1.

In the present application, the E1 sequences encoding the antigenic ectodomain of the E1 protein, which does not overlap the carboxyterminal signal-anchor sequences of E1 disclosed by Cha et al. (1992; WO 92/19743), in addition to the NS4 epitope region, and a part of the NS5 region are disclosed for 4 different isolates: BR33, BR34, BR36, HCCl53 and HD10, all belonging to type 3a (SEQ ID NO 1, 3, 5, 7, 9, 11, 13, 15, 17, 19, 21, 23, 25, 27, 29, 31, 35, 37 or 39).

Also within the present invention are new subtype 3c sequences (SEQ ID NO 147, 149 of the isolate BE98 in the Core and NS5 regions (see Figures 3 and 1).

Finally the present invention also relates to a new subtype 3a sequence as represented in SEQ ID NO 217 (see Figure 1)

Also included within the present invention are sequence variants of the polynucleic acids as selected from any of the nucleotide sequences as given in any of the above mentioned SEQ ID numbers, with said sequence variants containing either deletions and/or insertions of one or more nucleotides, mainly at the extremities of oligonucleotides (either 3' or 5'), or substitutions of some non-essential nucleotides by others (including modified nucleotides an/or inosine), for example, a type 1 or 2 sequence might be modified into a type 3 sequence by replacing some nucleotides of the type 1 or 2 sequence with type-specific nucleotides of type 3 as shown in Figure 1 (NSS region), Figure 3 (Core region), Figure 4 (Core/E1 region), Figure 6 and 10 (NS3/NS4 region).

According to another embodiment, the present invention relates to a polynucleic acid composition as defined above, wherein said polynucleic acids correspond to a nucleotide sequence selected from any of the following HCV type 5 genomic sequences:

- an HCV genomic sequence as having a homology of more than 85%, preferably more than 86%, most preferably more than 87% homology to any of the sequences as represented in SEQ ID NO 41, 43, 45, 47, 49, 51, 53 (PC sequences) or 151 (BE95 sequence) in the region spanning positions 1 to 573 of the Core region as shown in Figure 9 and 3;
- an HCV genomic sequence as having a homology of more than 61%, preferably more than 63%, more preferably more than 65% homology, even more preferably more than 66% homology and most preferably more than 67% homology (f.i. 69 and 71%) to any of the sequences as represented in SEQ ID NO 41, 43, 45, 47, 49, 51, 53 (PC sequences), 153 or 155 (BE95, BE100 sequences) in the region spanning positions 574 to 957 of the E1 region as shown in Figure 4;
- an HCV genomic sequence having a homology of more than 76.5%, preferably of more than 77%, most preferably of more than 78% homology with any of the sequences as represented in SEQ ID NO 55, 57, 197 or 199 (PC sequences) in the region spanning positions 3856 to 4209 of the NS3 region as shown in Figure 6 or 10;
- an HCV genomic sequence having a homology of more than 68%, preferably of more than 70%, most preferably of more than 72% homology with the sequence as represented in SEQ ID NO 157 (BE95 sequence) in the region spanning positions 980 to 1179 of the E1/E2 region as shown in Figure 13;
- an HCV genomic sequence having a homology of more than 57%, preferably more than

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59%, most preferably more than 61% homology to any of the sequences as represented in SEQ ID NO 59 or 61 (PC sequences) in the region spanning positions 4936 to 5296 of the NS4 region as shown in Figure 6 or 10:

- an HCV genomic sequence as having a homology of more than 93%, preferably more than 93.5%, most preferably more than 94% homology to any of the sequences as represented in SEQ ID NO 159 or 161 (BE95 or BE96 sequences) in the region spanning positions 7932 to 8271 of the NSSB region as shown in Figure 1.

Preferentially the above-mentioned genomic HCV sequences depict sequences from the coding regions of all the above-mentioned sequences.

According to the nucleotide distance classification system (with said nucleotide distances being calculated as explained above), said sequences of said composition are selected from:

- a nucleotide distance of less than 0.53, preferably less than 0.51, more preferably less than
 0.49 for the E1 region to the type 5 sequences depicted above;
- a nucleotide distance of less than 0.3, preferably less than 0.28, more preferably of less than 0.26 for the Core region to the type 5 sequences depicted above;
- a nucleotide distance of less than 0.072, preferably less than 0.071, more preferably less than 0.070 for the NS5B region to the type 5 sequences as depicted above.

Isolates with similar sequences in the 5'UR to a group of isolates including SA1, SA3, and SA7 described in the 5'UR by Bukh et al. (1992), have been reported and described in the 5'UR and NS5 region as group V by Cha et al. (1992; WO 92/19743). This group of isolates belongs to type 5a as described in the present invention (SEQ ID NO 41, 43, 45, 47, 49, 51, 53, 55, 57, 59, 61, 151, 153, 155, 157, 159, 161, 197 and 199).

Also included within the present invention are sequence variants of the polynucleic acids as selected from any of the nucleotide sequences as given in any of the above given SEQ ID numbers with said sequence variants containing either deletion and/or insertions of one or more nucleotides, mainly at the extremities of oligonucleotides (either 3' or 5'), or substitutions of some non-essential nucleotides (i.e. nucleotides not essential to discriminate between different genotypes of HCV) by others (including modified nucleotides and/or inosine), for example, a type 1 or 2 sequence might be modified into a type 5 sequence by replacing some nucleotides of the type 1 or 2 sequence with type-specific nucleotides of type 5 as shown in Figure 3 (Core region), Figure 4 (Core/EI region), Figure 10 (NS3 / NS4 region), Figure 14 (El1/E2 region),

Another group of isolates including BU74 and BU79 having similar sequences in the 5'UR to isolates including Z6 and Z7 as described in the 5'UR by Bukh et al. (1992), have been described in the 5'UR and classified as a new type 4 by the inventors of this application (Stuyver et al., 1993). Coding sequences, including core, E1 and NS5 sequences of several new Gabonese isolates belonging to this group, are disclosed in the present invention (SEQ ID NO 106, 108, 110, 112, 114, 116, 118, 120 and 122).

According to yet another embodiment, the present invention relates to a composition as defined above, wherein said polynucleic acids correspond to a nucleotide sequence selected from any of the following HCV type 4 genomic sequences:

- an HCV genomic sequence having a homology of more than 66%, preferably more than 68%, most preferably more than 70% homology in the E1 region spanning positions 574 to 957 to any of the sequences as represented in SEQ ID NO 118, 120 or 122 (GB358, GB549, GB809 sequences) as shown in Figure 4;
- an HCV genomic sequence having a homology of more than 71%, preferably more than 72%, most preferably more than 74% homology to any of the sequences as represented in SEQ ID NO 118, 120 or 122 (GB358, GB549, GB809 sequences) in the region spanning positions 379 to 957 of the E1 region as shown in Figure 4;
- an HCV genomic sequence having a homology of more than 92%, preferably more than 93%, most preferably more than 94% homology to any of the sequences as represented in SEQ ID NO 163 or 165 (GB809, CAM600 sequences) in the region spanning positions 1 to 378 of the Core/E1 region as shown in Figure 4;
- an HCV genomic sequence (subtype 4c) having a homology of more than 85%, preferably more than 86%, more preferably more than 86.5% homology, most preferably more than 87, more than 88 or more than 89% homology to any of the sequences as represented in SEQ ID NO 183, 185 or 187 (GB116, GB215, GB809 sequences) in the region spanning positions 379 to 957 of the E1 region as shown in Figure 4;
- an HCV genomic sequence (subtype 4a) having a homology of more than 81%, preferably more than 83%, most preferably more than 85% homology to the sequence as represented in SEQ ID NO 189 (GB908 sequence) in the region spanning positions 379 to 957 of the E1 region as shown in Figure 4;
- an HCV genomic sequence (subtype 4e) having a homology of more than 85%, preferably more than 87%, most preferably more than 89% homology to any of the sequences as represented in SEQ ID NO 167 or 169 (CAM600, GB908 sequences) in the region

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spanning positions 379 to 957 of the E1 region as shown in Figure 4;

- an HCV genomic sequence (subtype 4f) having a homology of more than 79%, preferably more than 81%, most preferably more than 83% homology to any of the sequences as represented in SEQ ID NO 171 or 173 (CAMG22, CAMG27 sequences) in the region spanning positions 379 to 957 of the E1 region as shown in Figure 4;

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- an HCV genomic sequence (subtype 4g) having a homology of more than 84%, preferably
 more than 86%, most preferably more than 88% homology to the sequence as represented
 in SEQ ID NO 175 (GB549 sequence) in the region spanning positions 379 to 957 of the
 E1 region as shown in Figure 4;
- an HCV genomic sequence (subtype 4h) having a homology of more than 83%, preferably
 more than 85%, most preferably more than 87% homology to the sequence as represented
 in SEQ ID NO 177 (GB438 sequence) in the region spanning positions 379 to 957 of the
 E1 region as shown in Figure 4;
- an HCV genomic sequence (subtype 4i) as having a homology of more than 76%, preferably more than 78%, most preferably more than 80% homology to the sequence as represented in SEQ ID NO 179 (CAR4/1205 sequence) in the region spanning positions 379 to 957 of the E1 region as shown in Figure 4;
- an HCV genomic sequence (subtype 4j?) having a homology of more than 84%, preferably more than 86%, most preferably more than 88% homology to the sequence as represented in SEQ ID NO 181 (CAR4/901 sequence) in the region spanning positions 379 to 957 of the E1 region as shown in figure 4;
- an HCV genomic sequence as having a homology of more than 73%, preferably more than 75%, most preferably more than 77% homology to any of the sequences as represented in SEQ ID NO 106, 108, 110, 112, 114, or 116 (GB48, GB116, GB215, GB358, GB549, GB809 sequences) in the region spanning positions 7932 to 8271 of the NS5 region as shown in figure 1:
- an HCV genomic sequence (subtype 4c) having a homology of more than 88%, preferably more than 89%, most preferably more than 90% homology to any of the sequences as represented in SEQ ID NO 106, 108, 110, or 112 (GB48, GB116, GB215, GB358 sequences) in the region spanning positions 7932 to 8271 of the NS5 region as shown in Figure 1;
- an HCV genomic sequence (subtype 4e) having a homology of more than 88%, preferably more than 89%, most preferably more than 90% homology to any of the sequences as

represented in SEQ ID NO 116 or 201 (GB809 or CAM 600 sequences) in the region spanning positions 7932 to 8271 of the NS5 region as shown in Figure 1;

- an HCV genomic sequence (subtype 4f) having a homology of more than 87%, preferably
 more than 89%, most preferably more than 90% homology to the sequence as represented
 in SEQ ID NO 203 (CAMG22 sequence) in the region spanning positions 7932 to 8271
 of the NS5 region as shown in Figure 1;
- an HCV genomic sequence (subtype 4g) as having a homology of more than 85%, preferably more than 87%, most preferably more than 89% homology to the sequence as represented in SEQ ID NO 114 (GB549 sequence) in the region spanning positions 7932 to 8271 of the NS5 region as shown in Figure 1;
- an HCV genomic sequence (subtype 4h) as having a homology of more than 86%, preferably more than 87%, more preferably more than 88% homology, more preferably more than 89% homology to the sequence as represented in SEQ ID NO 207 (GB437 sequence) in the region spanning positions 7932 to 8271 of the NSS region as shown in Figure 1;
- an HCV genomic sequence (subtype 4i) having a homology of more than 84%, preferably
 more than 86%, most preferably more than 88% homology to the sequence as represented
 in SEQ ID NO 209 (CAR4/1205 sequence) in the region spanning positions 7932 to 8271
 of the NSS region as shown in figure 1;
- an HCV genomic sequence (subtype 4j) having a homology of more than 81%, preferably more than 83%, most preferably more than 85% homology to the sequence as represented in SEQ ID NO 211 (CAR1/501 sequence) in the region spanning positions 7932 to 8271 of the NS5 region as shown in figure 1.

Preferentially the above-mentioned genomic HCV sequences depict sequences from the coding regions of all the above-mentioned sequences.

According to the nucleotide distance classification system (with said nucleotide distances being calculated as explained above), said sequences of said composition are selected from:

- an HCV genomic sequence (type 4) being characterized as having a nucleotide distance of less than 0.52, 0.50, 0.4880, 0.46, 0.44, 0.43 or most preferably less than 0.42 in the region spanning positions 574 to 957 to any of the sequences as represented in SEQ ID NO 118, 120 or 122 in the region spanning positions 1 to 957 of the Core/E1 region as shown in Figure 4;
- an HCV genomic sequence (type 4) being characterized as having a nucleotide distance of

- less than 0.39, 0.36 0.34 0.32 or most preferably less than 0.31 to any of the sequences as represented in SEQ ID NO 118, 120 or 122 in the region spanning positions 379 to 957 of the E1 region as shown in Figure 4:
- an HCV genomic sequence (subtype 4c) being characterized as having a nucleotide distance of less than 0.27, 0.26, 0.24, 0.22, 0.20, 0.18, 0.17, 0.162, 0.16 or most preferably less than 0.15 to any of the sequences as represented in SEQ ID NO 183, 185 or 187 in the region spanning positions 379 to 957 of the E1 region as shown in Figure 4;
- an HCV genomic sequence (subtype 4a) being characterized as having a nucleotide distance of less than 0.30, 0.28, 0.26, 0.24, 0.22, 0.21 or most preferably of less than 0.205 to the sequence as represented in SEQ ID NO 189 in the region spanning positions 379 to 957 of the E1 region as shown in Figure 4;
- an HCV genomic sequence (subtype 4e) being characterized as having a nucleotide distance of less than 0.26, 0.25, 0.23, 0.21, 0.19, 0.17, 0.165, most preferably less than 0.16 to any of the sequences as represented in SEQ ID NO 167 or 169 in the region spanning positions 379 to 957 of the E1 region as shown in Figure 4;
- an HCV genomic sequence (subtype 4f) being characterized as having a nucleotide distance
 of less than 0.26, 0.24, 0.22, 0.20, 0.18, 0.16, 0.15 or most preferably less than 0.14 to
 any of the sequences as represented in SEQ ID NO 171 or 173 in the region spanning
 positions 379 to 957 of the E1 region as shown in Figure 4;
- an HCV genomic sequence (subtype 4g) being characterized as having a nucleotide distance of less than 0.20, 0.19, 0.18, 0.17 or most preferably of less than 0.16 to the sequence as represented in SEQ ID NO 175 in the region spanning positions 379 to 957 of the E1 region as shown in Figure 4;
- an HCV genomic sequence (subtype 4h) being characterized as having a nucleotide distance of less than 0.20, 0.19, 0.18, 0.17 and most preferably of less than 0.16 to the sequence as represented in SEQ ID NO 177 in the region spanning positions 379 to 957 of the E1 region as shown in Figure 4;
- an HCV genomic sequence (subtype 4i) being characterized as having a nucleotide distance of less than 0.27, 0.25, 0.23, 0.21 and preferably less than 0.16 to the sequence as represented in SEQ ID NO 179 in the region spanning positions 379 to 957 of the E1 region as shown in Figure 4;
- an HCV genomic sequence (subtype 4j?) being characterized as having a nucleotide distance of less than 0.19, 0.18, 0.17, 0.165 and most preferably of less than 0.16 to the

- sequence as represented in SEQ ID NO 181 in the region spanning positions 379 to 957 of the E1 region as shown in figure 4;
- an HCV genomic sequence (type 4) being characterized as having a nucleotide distance of less than 0.35, 0.34, 0.32 and most preferably of less than 0.30 to any of the sequences as represented in SEQ ID NO 106, 108, 110, 112, 114, or 116 in the region spanning positions 7932 to 8271 of the NS5 region as shown in figure 1;
- an HCV genomic sequence (subtype 4c) being characterized as having a nucleotide distance of less than 0.18, 0.16, 0.14, 0.135, 0.13, 0.1275 or most preferably less than 0.125 to any of the sequences as represented in SEQ ID NO 106, 108, 110, or 112 in the region spanning positions 7932 to 8271 of the NS5 region as shown in Figure 1;
- an HCV genomic sequence (subtype 4e) being characterized as having a nucleotide distance of less than 0.15, 0.14, 0.135, 0.13 and most preferably of less than 0.125 to any of the sequences as represented in SEQ ID NO 116 or 201 in the region spanning positions 7932 to 8271 of the NS5 region as shown in Figure 1;
- an HCV genomic sequence (subtype 4f) being characterized as having a nucleotide distance
 of less than 0.15, 0.14, 0.135, 0.13 or most preferably less than 0.125 to the sequence as
 represented in SEQ ID NO 203 in the region spanning positions 7932 to 8271 of the NS5
 region as shown in Figure 1;
- an HCV genomic sequence (subtype 4g) being characterized as having a nucleotide distance of less than 0.17, 0.16, 0.15, 0.14, 0.13 or most preferably less than 0.125 to the sequence as represented in SEQ ID NO 114 in the region spanning positions 7932 to 8271 of the NS5 region as shown in Figure 1;
- an HCV genomic sequence (subtype 4h) being characterized as having a nucleotide distance of less than 0.155, 0.15, 0.145, 0.14, 0.135, 0.13 or most preferably less than 0.125 to the sequence as represented in SEQ ID NO 207 in the region spanning positions 7932 to 8271 of the NS5 region as shown in Figure 1;
- an HCV genomic sequence (subtype 4i) being characterized as having a nucleotide distance of less than 0.17, 0.16, 0.15, 0.14, 0.13 or most preferably of less than 0.125 to the sequence as represented in SEQ ID NO 209 in the region spanning positions 7932 to 8271 of the NS5 region as shown in figure 1;
- an HCV genomic sequence (subtype 4j) being characterized as having a nucleotide distance of less than 0.21, 0.20, 0.19, 0.18, 0.17, 0.16, 0.15, 0.14, 0.13 and most preferably of less than 0.125 to the sequence as represented in SEQ ID NO 211 in the region spanning

positions 7932 to 8271 of the NS5 region as shown in figure 1.

Also included within the present invention are sequence variants of the polynucleic acids as selected from any of the nucleotide sequences as given in any of the above given SEQ ID numbers with said sequence variants containing either deletion and/or insertions of one or more nucleotides, mainly at the extremities of oligonucleotides (either 3' or 5'), or substitutions of some non-essential nucleotides (i.e. nucleotides not essential to discriminate between different genotypes of HCV) by others (including modified nucleotides an/or inosine), for example, a type 1 or 2 sequence might be modified into a type 4 sequence by replacing some nucleotides of the type 1 or 2 sequence with type-specific nucleotides of type 4 as shown in Figure 3 (Core region), Figure 4 (Core/E1 region), Figure 10 (NS3 / NS4 region), Figure 14 (E1/E2 region).

The present invention also relates to a sequence as represented in SEQ ID NO 193 (GB724 sequence).

After aligning NS5 or E1 sequences of GB48, GB, 116, GB215, GB358, GB549 and GB809, these isolates clearly segregated into 3 subtypes within type 4: GB48, GB116, GB215 and GB358 belong to the sybtype designated 4c, GB549 to subtype 4g and GB809 to subtype 4e. In NS5, GB809 (subtype 4e) showed a higher nucleic acids homology to subtype 4c isolates (85.6 - 86.8%) than to GB549 (subtype 4g, 79.7%), while GB549 showed similar homologies to both other subtypes (78.8 to 80% to subtype 4c and 79.7% to subtype 4e). In E1, subtype 4c showed equal nucleic acid homologies of 75.2% to subtypes 4g and 4e while 4g and 4e were 78.4% homologous. At the amino acid level however, subtype 4e showed a normal homology to subtype 4c (80.2%), while subtype 4g was more homologous to 4c (83.3%) and 4e (84.1%).

According to yet another embodiment, the present invention relates to a composition as defined above, wherein said polynucleic acids correspond to a nucleotide sequence selected from any of the following HCV type 2d genomic sequences:

- an HCV genomic sequence as having a homology of more than 78%, preferably more than 80%, most preferably more than 82% homology to the sequence as represented in SEQ ID NO (NE92) 143 in the region spanning positions 379 to 957 of the Core/E1 region as shown in Figure 4;
- an HCV genomic sequence as having a homology of more than 74%, preferably more than 76%, most preferably more than 78% homology to the sequence as represented in SEQ ID NO 143 (NE92) in the region spanning positions 574 to 957 as shown in Figure 4;

- an HCV genomic sequence as having a homology of more than 87%, preferably more than 89%, most preferably more than 91% homology to the sequence as represented in SEQ ID NO 145 (NE92) in the region spanning positions 7932 to 8271 of the NS5B region as shown in Figure 1.

Preferentially the above-mentioned genomic HCV sequences depict sequences from the coding regions of all the above-mentioned sequences.

According to the nucleotide distance classification system (with said nucleotide distances being calculated as explained above), said sequences of said composition are selected from:

- a nucleotide distance of less than 0.32, preferably less than 0.31, more preferably less than
 0.30 for the E1 region (574 to 957) to any of the above specified sequences;
- a nucleotide distance of less than 0.08, preferably less than 0.07, more preferably less than
 0.06 for the Core region (1 to 378) to any of the above given sequences
- a nucleotide distance of less than 0.15, preferantially less than 0.13, more preferentially less than 0.12 for the NSSB region to any of the above-specified sequences.

Polynucleic acid sequences according to the present invention which are homologous to the sequences as represented by a SEQ ID NO can be characterized and isolated according to any of the techniques known in the art, such as amplification by means of type or subtype specific primers, hybridization with type or subtype specific probes under more or less stringent conditions, serological screening methods (see examples 4 and 11) or via the LiPA typing system.

Polynucleic acid sequences of the genomes indicated above from regions not yet depicted in the present examples, figures and sequence listing can be obtained by any of the techniques known in the art, such as amplification techniques using suitable primers from the type or subtype specific sequences of the present invention.

The present invention relates also to a composition as defined above, wherein said polynucleic acid is liable to act as a primer for amplifying the nucleic acid of a certain isolate belonging to the genotype from which the primer is derived.

An example of a primer according to this embodiment of the invention is HCPr 152 as shown in table 7 (SEO ID NO 79).

The term "primer" refers to a single stranded DNA oligonucleotide sequence capable of acting as a point of initiation for synthesis of a primer extension product which is complementary to the nucleic acid strand to be copied. The length and the sequence of the primer must be such that they allow to prime the synthesis of the extension products.

Preferably the primer is about 5-50 nucleotides. Specific length and sequence will depend on the complexity of the required DNA or RNA targets, as well as on the conditions of primer use such as temperature and ionic strength.

The fact that amplification primers do not have to match exactly with corresponding template sequence to warrant proper amplification is amply documented in the literature (Kwok et al., 1990).

The amplification method used can be either polymerase chain reaction (PCR; Saiki et al., 1988), ligase chain reaction (LCR; Landgren et al., 1988; Wu & Wallace, 1989; Barany, 1991), nucleic acid sequence-based amplification (NASBA; Guatelli et al., 1990; Compton, 1991), transcription-based amplification system (TAS; Kwoh et al., 1989), strand displacement amplification (SDA; Duck, 1990; Walker et al., 1992) or amplification by means of QB replicase (Lizardi et al., 1988; Lomeli et al., 1989) or any other suitable method to amplify nucleic acid molecules using primer extension. During amplification, the amplified products can be conveniently labelled either using labelled primers or by incorporating labelled nucleotides. Labels may be isotopic (²²P, ³⁵S, etc.) or non-isotopic (biotin, digoxigenin, etc.). The amplification reaction is repeated between 20 and 80 times, advantageously between 30 and 50 times.

The present invention also relates to a composition as defined above, wherein said polynucleic acid is able to act as a hybridization probe for specific detection and/or classification into types of a nucleic acid containing said nucleotide sequence, with said oligonucleotide being possibly labelled or attached to a solid substrate.

The term "probe" refers to single stranded sequence-specific oligonucleotides which have a sequence which is complementary to the target sequence of the HCV genotype(s) to be detected.

Preferably, these probes are about 5 to 50 nucleotides long, more preferably from about 10 to 25 nucleotides.

The term "solid support" can refer to any substrate to which an oligonucleotide probe can be coupled, provided that it retains its hybridization characteristics and provided that the background level of hybridization remains low. Usually the solid substrate will be a microtiter plate, a membrane (e.g. nylon or nitrocellulose) or a microsphere (bead). Prior to application to the membrane or fixation it may be convenient to modify the nucleic acid probe in order to facilitate fixation or improve the hybridization efficiency. Such modifications may encompass homopolymer tailing, coupling with different reactive groups such as aliphatic

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groups, NH₂ groups, SH groups, carboxylic groups, or coupling with biotin or haptens.

The present invention also relates to the use of a composition as defined above for detecting the presence of one or more HCV genotypes, more particularly for detecting the presence of a nucleic acid of any of the HCV genotypes having a nucleotide sequence as defined above, present in a biological sample liable to contain them, comprising at least the following steps:

- (i) possibly extracting sample nucleic acid,
- (ii) possibly amplifying the nucleic acid with at least one of the primers as defined above or any other HCV subtype 2d, HCV type 3, HCV type 4, HCV type 5 or universal HCV primer,
- (iii) hybrizing the nucleic acids of the biological sample, possibly under denatured conditions, and with said nucleic acids being possibly labelled during or after amplification, at appropriate conditions with one or more probes as defined above, with said probes being preferably attached to a solid substrate.
- (iv) washing at appropriate conditions,
- (v) detecting the hybrids formed.
- inferring the presence of one or more HCV genotypes present from the observed hybridization pattern.

Preferably, this technique could be performed in the Core or NS5B region.

The term "nucleic acid" can also be referred to as analyte strand and corresponds to a single- or double-stranded nucleic acid molecule. This analyte strand is preferentially positive-or negative stranded RNA, cDNA or amplified cDNA.

The term "biological sample" refers to any biological sample (tissue or fluid) containing HCV nucleic acid sequences and refers more particularly to blood serum or plasma samples.

The term "HCV subtype 2d primer" refers to a primer which specifically amplifies HCV subtype 2d sequences present in a sample (see Examples section and figures).

The term "HCV type 3 primer" refers to a primer which specifically amplifies HCV type 3 sequences present in a sample (see Examples section and figures).

The term "HCV type 4 primer" refers to a primer which specifically amplifies HCV type 4 genomes present in a sample.

The term "universal HCV primer" refers to oligonucleotide sequences complementary to any of the conserved regions of the HCV genome.

The term "HCV type 5 primer" refers to a primer which specifically amplifies HCV type

5 genomes present in a sample. The term "universal HCV primer" refers to oligonucleotide sequences complementary to any of the conserved regions of the HCV genome.

The expression "appropriate" hybridization and washing conditions are to be understood as stringent and are generally known in the art (e.g. Maniatis et al., Molecular Cloning: A Laboratory Manual, New York, Cold Spring Harbor Laboratory, 1982).

However, according to the hybridization solution (SSC, SSPE, etc.), these probes should be hybridized at their appropriate temperature in order to attain sufficient specificity.

The term "labelled" refers to the use of labelled nucleic acids. This may include the use of labelled nucleotides incorporated during the polymerase step of the amplification such as illustrated by Saiki et al. (1988) or Bej et al. (1990) or labelled primers, or by any other method known to the person skilled in the art.

The process of the invention comprises the steps of contacting any of the probes as defined above, with one of the following elements:

- either a biological sample in which the nucleic acids are made available for hybridization,
- or the purified nucleic acids contained in the biological sample
- or a single copy derived from the purified nucleic acids,
- or an amplified copy derived from the purified nucleic acids, with said elements or with said probes being attached to a solid substrate.

The expression "inferring the presence of one or more HCV genotypes present from the observed hybridization pattern" refers to the identification of the presence of HCV genomes in the sample by analyzing the pattern of binding of a panel of oligonucleotide probes. Single probes may provide useful information concerning the presence or absence of HCV genomes in a sample. On the other hand, the variation of the HCV genomes is dispersed in nature, so rarely is any one probe able to identify uniquely a specific HCV genome. Rather, the identity of an HCV genotype may be inferred from the pattern of binding of a panel of oligonucleotide probes, which are specific for (different) segments of the different HCV genomes. Depending on the choice of these oligonucleotide probes, each known HCV genotype will correspond to a specific hybridization pattern upon use of a specific combination of probes. Each HCV genotype will also be able to be discriminated from any other HCV genotype amplified with the same primers depending on the choice of the oligonucleotide probes. Comparison of the generated pattern of positively hybridizing probes for a sample containing one or more unknown HCV sequences to a scheme of expected

hybridization patterns, allows one to clearly infer the HCV genotypes present in said sample.

The present invention thus relates to a method as defined above, wherein one or more hybridization probes are selected from any of SEQ ID NO 1, 3, 5, 7, 9, 11, 13, 15, 17, 19, 21, 23, 25, 27, 29, 31, 33, 35, 37, 39, 41, 43, 45, 47, 49, 51, 53, 55, 57, 59 or 61, 106, 108, 110, 112, 114, 116, 118, 120, 122, 143, 145, 147, 149, 151, 153, 155, 157, 159, 161, 163, 165, 167, 169, 171, 173, 175, 177, 179, 181, 183, 185, 187, 198, 191, 193, 195, 197, 199, 201, 203, 205, 207, 209, 211, 213, 215, 217, 222, 269 or sequence variants thereof, with said sequence variants containing deletions and/or insertions of one or more nucleotides, mainly at their extremities (either 3' or 5'), or substitutions of some non-essential nucleotides (i.e. nucleotides not essential to discriminate between genotypes) by others (including modified nucleotides or inosine), or with said variants consisting of the above-mentioned oligonucleotide probes, or with said variants consisting of ribonucleotides instead of deoxyribonucleotides, all provided that said variant probes can be caused to hybridize with the same specificity as the oligonucleotide probes from which they are derived.

In order to distinguish the amplified HCV genomes from each other, the target polynucleic acids are hybridized to a set of sequence-specific DNA probes targetting HCV genotypic regions located in the HCV polynucleic acids.

Most of these probes target the most type-specific regions of HCV genotypes, but some can be caused to hybridize to more than one HCV genotype.

According to the hybridization solution (SSC, SSPE, etc.), these probes should be stringently hybridized at their appropriate temperature in order to attain sufficient specificity. However, by slightly modifying the DNA probes, either by adding or deleting one or a few nucleotides at their extremities (either 3' or 5'), or substituting some non-essential nucleotides (i.e. nucleotides on tessential to discriminate between types) by others (including modified nucleotides or inosine) these probes or variants thereof can be caused to hybridize specifically at the same hybridization conditions (i.e. the same temperature and the same hybridization solution). Also changing the amount (concentration) of probe used may be beneficial to obtain more specific hybridization results. It should be noted in this context, that probes of the same length, regardless of their GC content, will hybridize specifically at approximately the same temperature in TMACI solutions (Jacobs et al., 1988).

Suitable assay methods for purposes of the present invention to detect hybrids formed between the oligonucleotide probes and the nucleic acid sequences in a sample may comprise any of the assay formats known in the art, such as the conventional dot-blot format, sandwich hybridization or reverse hybridization. For example, the detection can be accomplished using a dot blot format, the unlabelled amplified sample being bound to a membrane, the membrane being incorporated with at least one labelled probe under suitable hybridization and wash conditions, and the presence of bound probe being monitored.

An alternative and preferred method is a "reverse" dot-blot format, in which the amplified sequence contains a label. In this format, the unlabelled oligonucleotide probes are bound to a solid support and exposed to the labelled sample under appropriate stringent hybridization and subsequent washing conditions. It is to be understood that also any other assay method which relies on the formation of a hybrid between the nucleic acids of the sample and the oligonucleotide probes according to the present invention may be used.

According to an advantageous embodiment, the process of detecting one or more HCV genotypes contained in a biological sample comprises the steps of contacting amplified HCV nucleic acid copies derived from the biological sample, with oligonucleotide probes which have been immobilized as parallel lines on a solid support.

According to this advantageous method, the probes are immobilized in a Line Probe Assay (LiPA) format. This is a reverse hybridization format (Saiki et al., 1989) using membrane strips onto which several oligonucleotide probes (including negative or positive control oligonucleotides) can be conveniently applied as parallel lines.

The invention thus also relates to a solid support, preferably a membrane strip, carrying on its surface, one or more probes as defined above, coupled to the support in the form of parallel lines.

The LiPA is a very rapid and user-friendly hybridization test. Results can be read 4 h. after the start of the amplification. After amplification during which usually a non-isotopic label is incorporated in the amplified product, and alkaline denaturation, the amplified product is contacted with the probes on the membrane and the hybridization is carried out for about 1 to 1,5 h hybridized polynucleic acid is detected. From the hybridization pattern generated, the HCV type can be deduced either visually, but preferably using dedicated software. The LiPA format is completely compatible with commercially available scanning devices, thus rendering automatic interpretation of the results very reliable. All those advantages make the LiPA format liable for the use of HCV detection in a routine setting. The LiPA format should be particularly advantageous for detecting the presence of different HCV genotypes.

The present invention also relates to a method for detecting and identifying novel HCV

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genotypes, different from the known HCV genomes, comprising the steps of:

 determining to which HCV genotype the nucleotides present in a biological sample belong, according to the process as defined above,

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 in the case of observing a sample which does not generate a hybridization pattern compatible with those defined in Table 3, sequencing the portion of the HCV genome sequence corresponding to the aberrantly hybridizing probe of the new HCV genotype to be determined.

The present invention also relates to the use of a composition as defined above, for detecting one or more genotypes of HCV present in a biological sample liable to contain them, comprising the steps of:

- (i) possibly extracting sample nucleic acid,
- (ii) amplifying the nucleic acid with at least one of the primers as defined above,
- (iii) sequencing the amplified products
- (iv) inferring the HCV genotypes present from the determined sequences by comparison to all known HCV sequences.

The present invention also relates to a composition consisting of or comprising at least one peptide or polypeptide comprising a contiguous-sequence of at least 5 amino acids corresponding to a contiguous amino acid sequence encoded by at least one of the HCV genomic sequences as defined above, having at least one amino acid differing from the corresponding region of known HCV (type 1 and/or type 2 and/or type 3) polyprotein sequences as shown in Table 3, or muteins thereof.

It is to be noted that, at the level of the amino acid sequence, an amino acid difference (with respect to known HCV amino acid sequences) is necessary, which means that the polypeptides of the invention correspond to polynucleic acids having a nucleotide difference (with known HCV polynucleic acid sequences) involving an amino acid difference.

The new amino acid sequences, as deduced from the disclosed nucleotide sequences (see SEQ ID NO 1 to 62 and 106 to 123 and 143 to 218, 223 and 270), show homologies of only 59.9 to 78% with prototype sequences of type 1 and 2 for the NS4 region, and of only 53.9 to 68.8% with prototype sequences of type 1 and 2 for the EI region. As the NS4 region is known to contain several epitopes, for example characterized in patent application EP-A-0 489 968, and as the EI protein is expected to be subject to immune attack as part of the viral envelope and expected to contain epitopes, the NS4 and E1 epitopes of the new type 3, 4 and 5 isolates will consistently differ from the epitopes present in type 1 and 2 isolates. This is

examplified by the type-specificity of NS4 synthetic peptides as presented in example 4, and the type-specificity of recombinant E1 proteins in example 11.

After aligning the new subtype 2d, type 3, 4 and 5 (see SEQ ID NO 1 to 62 and 106 to 123 and 143 to 218, 223 and 270) amino acid sequences with the prototype sequences of type 1a, 1b, 2a, and 2b, type- and subtype-specific variable regions can be delineated as presented in Figure 5 and 7.

As to the muteins derived from the polypeptides of the invention, Table 4 gives an overview of the amino acid substitutions which could be the basis of some of the muteins as defined above.

The peptides according to the present invention contain preferably at least 5 contiguous HCV amino acids, preferably however at least 8 contiguous amino acids, at least 10 or at least 15 (for instance at least 9, 11, 12, 13, 14, 20 or 25 amino acids) of the new HCV sequences of the invention.

TABLE 4

Amino acids	cids Synonymous groups		
Ser (S)	Ser, Thr, Gly, Asn		
Arg (R)	Arg, His, Lys, Glu, Gln		
Leu (L)	Leu; Ile, Met, Phe, Val, Tyr		
Pro (P)	Pro, Ala, Thr, Gly		
Thr (T)	Thr, Pro, Ser, Ala, Gly, His, Gln		
Ala (A)	Ala, Pro, Gly, Thr		
Val (V)	Val, Met, Ile, Tyr, Phe, Leu, Val		
Gly (G)	Gly, Ala, Thr, Pro, Ser		
Ile (I)	Ile, Met, Leu, Phe, Val, Ile, Tyr		
Phe (F)	Phe, Met, Tyr, Ile, Leu, Trp, Val		
Tyr (Y)	Tyr, Phe, Trp, Met, Ile, Val, Leu		
Cys (C)	Cys, Ser, Thr, Met		
His (H)	His, Gln, Arg, Lys, Glu, Thr		
Gln (Q)	Gln, Glu, His, Lys, Asn, Thr, Arg		
Asn (N)	Asn, Asp, Ser, Gln		
Lys (K)	Lys, Arg, Glu, Gln, His		
Asp (D)	Asp, Asn, Glu, Gln		
Glu (E)	Glu, Gln, Asp, Lys, Asn, His, Arg		
Met (M)	Met, Ile, Leu, Phe, Val		

The polypeptides of the invention, and particularly the fragments, can be prepared by classical chemical synthesis.

The synthesis can be carried out in homogeneous solution or in solid phase.

For instance, the synthesis technique in homogeneous solution which can be used is the one described by Houbenweyl in the book entitled "Methode der organischen chemie" (Method of organic chemistry) edited by E. Wunsh, vol. 15-1 et II. THIEME, Stuttgart 1974.

The polypeptides of the invention can also be prepared in solid phase according to the methods described by Atherton and Shepard in their book entitled "Solid phase peptide synthesis" (IRL Press, Oxford, 1989).

The polypeptides according to this invention can be prepared by means of recombinant DNA techniques as described by Maniatis et al., Molecular Cloning: A Laboratory Manual, New York, Cold Spring Harbor Laboratory, 1982).

The present invention relates particularly to a polypeptide or peptide composition as defined above, wherein said contiguous sequence contains in its sequence at least one of the following amino acid residues:

L7. O43, M44, S60, R67, Q70, T71, A79, A87, N106, K115, A127, A190, S130, V134, G142, I144, E152, A157, V158, P165, S177 or Y177, I178, V180 or E180 or F182, R184, I186, H187, T189, A190, S191 or G191, Q192 or L192 or I192 or V192 or E192, N193 or H193 or P193, W194 or Y194, H195, A197 or I197 or V197 or T197, V202, I203 or L203, Q208, A210, V212, F214, T216, R217 or D217 or E217 or V217, H218 or N218, H219 or V219 or L219, L227 or I227, M231 or E231 or Q231, T232 or D232 or A232 or K232, Q235 or I235, A237 or T237, I242, I246, S247, S248, V249, S250 or Y250, I251 or V251 or M251 or F251, D252, T254 or V254, L255 or V255, E256 or A256, M258 or F258 or V258, A260 or Q260 or S260, A261, T264 or Y264, M265, I266 or A266, A267, G268 or T268. F271 or M271 or V271, I277, M280 or H280, I284 or A284 or L84, V274, V291, N292 or S292, R293 or I293 or Y293, O294 or R294, L297 or I297 or O297, A299 or K299 or O299, N303 or T303, T308 or L308, T310 or F310 or A310 or D310 or V310, L313, G317 or Q317, L333, S351, A358, A359, A363, S364, A366, T369, L373, F376, Q386, I387, S392, I399, F402, I403, R405, D454, A461, A463, T464, K484, O500, E501, S521, K522, H524, N528, S531, S532, V534, F536, F537, M539, I546, C1282, A1283, H1310. V1312, Q1321, P1368, V1372, V1373, K1405, Q1406, S1409, A1424, A1429, C1435, S1436, S1456, H1496, A1504, D1510, D1529, I1543, N1567, D1556, N1567, M1572, Q1579, L1581, S1583, F1585, V1595, E1606 or T1606, M1611, V1612 or L1612, P1630, C1636, P1651, T1656 or I1656, L1663, V1667, V1677, A1681, H1685, E1687, G1689. V1695, A1700, O1704, Y1705, A1713, A1714 or S1714, M1718, D1719, A1721 or T1721. R1722, A1723 or V1723, H1726 or G1726, E1730, V1732, F1735, I1736, S1737, R1738. T1739, G1740, Q1741, K1742, Q1743, A1744, T1745, L1746, E1747 or K1747, I1749. A1750, T1751 or A1751, V1753, N1755, K1756, A1757, P1758, A1759, H1762, T1763, Y1764, P2645, A2647, K2650, K2653 or L2653, S2664, N2673, F2680, K2681, L2686, H2692, Q2695 or L2695 or I2695, V2712, F2715, V2719 or Q2719, T2722, T2724, S2725. R2726, G2729, Y2735, H2739, I2748, G2746 or I2746, I2748, P2752 or K2752, P2754 or T2754, T2757 or P2757.

with said notation being composed of a letter representing the amino acid residue by its oneletter code, and a number representing the amino acid numbering according to Kato et al., 1990 as shown in Table 1 (comparison with other isolates). See also the numbering in Figures 2, 5, 7, and 11 (alignment amino acid sequences).

Within the group of unique and new amino acid residues of the present invention, the following residues were found to be specific for the following types of HCV according to the HCV classification system used in the present invention:

- Q208, R217, E231, I235, I246, T264, I266, A267, F271, K299, L2686, Q2719
 which are specific for the HCV subtype 2d sequences of the present invention as shown in Fig. 5 and 2;
- Q43, S60, R67, F182, I186, H187, A190, S191, L192, W194, V202, L203, V219,
 Q231, D232, A237, T254, M280, Q299, T303, L308, and/or L313 which are specific for the Core/E1 region of HCV type 3 of the invention as shown in Fig.
 5;
- D1556, Q1579, L1581, S1584, F1585, E1606, V1612, P1630, C1636, T1656,
 L1663, H1685, E1687, G1689, V1695, Y1705, A1713, A1714, A1721, V1723,
 H1726, R1738, Q1743, A1744, E1747, I1749, A1751, A1759 and/or H1762 which are specific for the NS3/4 region of HCV type 3 sequences of the invention as shown in Fig. 7;
- K2665, D2666, R2670 which are specific for the NS5B region of HCV type 3 of the invention as shown in Fig. 2;
- L7, A79, A127, S130, E152, V158, S177 or Y177, V180 or E180, R184, T189, Q192 or E192 or I192, N193 or H193, I197 or V197, I203, A210, V212, E217, H218, H219, L227, A232, V249, I251 or M251, D252, L255 or V255, E256, M258 or V258 or F258, A260 or Q260, M265, T268, V271, V274, M280, I284, N292 or S292, Q294, L297 or I297, T308, A310 or D310 or V310 or T310, and G317 which are specific for the core/E1 region of HCV type 4 sequences of the present invention as shown in Fig. 5;
- P2645, K2650, K2653, G2656, V2658, T2668, N2673 or N2673, K2681, H2686,
 D2691, L2692, Q2695 or L2695 or I2695, Y2704, V2712, F2715, V2719, I2722,
 S2725, G2729, Y2735, G2746 or I2746, P2752 or K2752, Q2753, P2754 or
 T2754, T2757 or P2757 which are specific for the NS5B region of the HCV type
 4 sequences of the present invention as shown in Fig. 2;
- M44, Q70, A87, N106, K115, V137, G142, P165, I178, F251, A299, N303, Q317
 which are specific for the Core/E1 region of the HCV type 4 sequences of the present invention as shown in Fig. 5;
- L333, S351, A358, A359, A363, S364, A366, T369, L373, F376, Q386, I387, S392, I399, F102, I403, R405, D454, A461, A463, T464, K484, Q500, E501, S521, K522, H524, N528, S532, V534, F537, M539, I546 which are specific for

- the E1/E2 region of the HCV type 5 sequences of the present invention as shown in Fig. 12;
- C1282, A1283, V1312, Q1321, P1368, V1372, K1405, Q1406, S1409, A1424,
 A1429, C1435, S1436, S1456, H1496, A1504, D1510, D1529, 11543, N1567,
 M1572, V1595, T1606, M1611, L1612, I1656, V1667, A1681, A1700, A1713,
 S1714, M1718, D1719, T1721, R1722, A1723, G1726, F1735, I1736, S1737,
- T1739, G1740, K1742, T1745, L1746, K1747, A1750, V1753, N1755, A1757, D1758, T1763, and Y1764 which are specific for the NS3/NS4 region of HCV type 5 sequences of the invention as shown in Fig. 7;
- A2647, L2653, S2674, F2680, T2724, R2726, Y2730, H2739 which are specific for the NS5B region of the HCV type 5 sequences of the present invention as shown in Fig. 2;
- A256, P1631, V1677, Q1704, E1730, V1732, Q1741 and T1751 which are specific for the HCV type 3 and 5 sequences of the present invention as shown in Fig. 5 and 7;
- T71, A157, 1227, T237, T240, Y250, V251, S260, M271, T2673, T2722, 12748
 which are specific for the HCV type 3 and 4 sequences of the present invention as shown in Fig. 5 and 2,
- V192, Y194, A197, P249, S250, R294 which are specific for the HCV type 4 and 5 sequences of the present invention as shown in Fig. 5;
- I293 which is specific for the HCV type 4 and subtype 2d sequence of the present invention as shown in Fig. 5:
- D217 and R294 which are specific for the HCV type 3, 4 and 5 sequences of the present invention as shown in Fig. 5;
- L192 which is specific for the HCV type 3 and subtype 2d sequences of the present invention as shown in Fig. 5;
- G191 and T197 which are specific for the HCV type 3, 4 and subtype 2d sequences
 of the present invention as shown in Fig. 5;
- K232 which is specific for the HCV subtype 2d en type 5 sequences of the present invention as shown in Fig. 5.

and with said notation being composed of a letter, unambiguously representing the amino acid by its one-letter code, and a number representing the amino acid numbering according to Kato et al., 1990 (see also Table 1 for comparison with other isolates), as well as Figure 2 (NS5 region), Figure 5 (Core/E1 region), Figure 7 (NS3/NS4 region), Figure 12 (E1/E2 region). Some of the above-mentioned amino acids may be contained in type or subtype specific enitones.

For example M231 (detected in type 5) refers to a methionine at position 231. A glutamine (Q) is present at the same position 231 in type 3 isolates, whereas this position is occupied by an arginine in type 1 isolates and by a lysine (K) or asparagine (N) in type 2 isolates (see Figure 5).

The peptide or polypeptide according to this embodiment of the invention may be possibly labelled, or attached to a solid substrate, or coupled to a carrier molecule such as biotin, or mixed with a proper adjuvant.

The variable region in the core protein (V-CORE in Fig. 5) has been shown to be useful for serotyping (Machida et al., 1992). The sequence of the disclosed type 5 sequence in this region shows type-specific features. The peptide from amino acid 70 to 78 shows the following unique sequence for the sequences of the present inevntion (see figure 5):

QPTGRSWGQ (SEQ ID NO 93)

RSEGRTSWAQ (SEQ ID NO 220)

and RTEGRTSWAO (SEO ID NO 221)

Another preferred V-Core spanning region is the peptide spanning positions 60 to 78 of subtype 3c with sequence:

SRRQPIPRARRTEGRSWAQ (SEQ ID NO 268)

Five type-specific variable regions (V1 to V5) can be identified after aligning E1 amino acid sequences of the 4 genotypes, as shown in Figure 5.

Region V1 encompasses amino acids 192 to 203, this is the amino-terminal 10 amino acids of the E1 protein. The following unique sequences as shown in Fig. 5 can be deduced:

LEWRNTSGLYVL (SEQ ID NO 83)

VNYRNASGIYHI (SEQ ID NO 126)

OHYRNISGIYHV (SEO ID NO 127)

EHYRNASGIYHI (SEQ ID NO 128)

IHYRNASGIYHI (SEQ ID NO 224)

VPYRNASGIYHV (SEQ ID NO 84)

VNYRNASGIYHI (SEQ ID NO 225) VNYRNASGVYHI (SEQ ID NO 226)

VNYHNTSGIYHL (SEQ ID NO 227)

QHYRNASGIYHV (SEQ ID NO 228) QHYRNVSGIYHV (SEQ ID NO 229) IHYRNASDGYYI (SEQ ID NO 230)

LQVKNTSSSYMV (SEQ ID NO 231)

Region V2 encompasses amino acids 213 to 223. The following unique sequences can be found in the V2 region as shown in Figure 5:

VYEADDVILHT (SEO ID NO 85)

VYETEHHILHL (SEQ ID NO 129)

VYEADHHIMHL (SEQ ID NO 130)

VYETDHHILHL (SEQ ID NO 131)

VYEADNLILHA (SEQ ID NO 86)

VWQLRAIVLHV (SEQ ID NO 232)

VYEADYHILHL (SEQ ID NO 233)

VYETDNHILHL (SEQ ID NO 234)

VYETENHILHL (SEQ ID NO 235)

VFETVHHILHL (SEQ ID NO 236)

VFETEHHILHL (SEQ ID NO 237)

VFETDHHIMHL (SEQ ID NO 238) VYETENHILHL (SEO ID NO 239)

VYEADALILHA (SEQ ID NO 240)

Region V3 encompasses the amino acids 230 to 242. The following unique V3 region sequences can be deduced from Figure 5:

VQDGNTSTCWTPV (SEQ ID NO 87)

VQDGNTSACWTPV (SEQ ID NO 241)

VRVGNQSRCWVAL (SEQ ID NO 132)

VRTGNTSRCWVPL (SEQ ID NO 133)

VRAGNVSRCWTPV (SEQ ID NO 134)

EEKGNISRCWIPV (SEQ ID NO 242)

VKTGNQSRCWVAL (SEQ ID NO 243)

VRTGNQSRCWVAL (SEQ ID NO 244)

VKTGNQSRCWIAL (SEQ ID NO 245)

VKTGNVSRCWIPL (SEQ ID NO 247)

VKTGNVSRCWISL (SEQ ID NO 248)

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VRKDNVSRCWVOI (SEO ID NO 249)
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Region V4 encompasses the amino acids 248 to 257. The following unique V4 region sequences can be deduced from figure 5:

VRYVGATTAS (SEQ ID NO 89)

APYIGAPLES (SEO ID NO 135)

APYVGAPLES (SEQ ID NO 136)

AVSMDAPLES (SEQ ID NO 137)

APSLGAVTAP (SEQ ID NO 90)

APSFGAVTAP (SEQ ID NO 250)

VSQPGALTKG (SEQ ID NO 251)

VKYVGATTAS (SEQ ID NO 252)

APYIGAPVES (SEQ ID NO 253)

AQHLNAPLES (SEQ ID NO 254)

SPYVGAPLEP (SEQ ID NO 255)

SPYAGAPLEP (SEQ ID NO 256)

APYLGAPLEP (SEQ ID NO 257)

APYLGAPLES (SEQ ID NO 258) APYVGAPLES (SEQ ID NO 259)

VPYLGAPLTS (SEO ID NO 260)

APHLRAPLSS (SEQ ID NO 261)

APYLGAPLTS (SEQ ID NO 262)

Region V5 encompasses the amino acids 294 to 303. The following unique V5 region peptides can be deduced from figure 5:

RPRRHOTVOT (SEO ID NO 91)

QPRRHWTTQD (SEQ ID NO 138)

RPRRHWTTQD (SEQ ID NO 139)

RPRQHATVQN (SEQ ID NO 92)

RPRQHATVQD (SEQ ID NO 263)

SPQHHKFVQD (SEQ ID NO 264)

RPRRLWTTQE (SEQ ID NO 265)

PPRIHETTQD (SEQ ID NO 266)

The variable region in the E2 region (HVR-2) of type 5a as shown in Figure 12 spanning amino acid positions 471 to 484 is also a preferred peptide according to the present invention

with the following sequence:

TISYANGSGPSDDK (SEO ID NO 267)

The above given list of peptides are particularly suitable for vaccine and diagnostic development.

Also comprised in the present invention is any synthetic peptide or polypeptide containing at least 5 contiguous amino acids derived from the above-defined peptides in their peptidic chain.

According to a specific embodiment, the present invention relates to a composition as defined above, wherein said contiguous sequence is selected from any of the following HCV amino acid type 3 sequences:

- a sequence having a homology of more than 72%, preferably more than 74%, more preferably more than 77% and most preferably more than 80 or 84% homology to any of the amino acid sequences as represented in SEQ ID NO 14, 16, 18, 20, 22, 24, 26 or 28 (HD10, BR36, BR33 sequences) in the region spanning positions 140 to 319 in the Core/E1 region as shown in Figure 5;
- a sequence having a homology of more than 70%, preferably more than 72%, more preferably more than 75% homology, most preferably more than 81% homology to any of the amino acid sequences as represented in SEQ ID NO 14, 16, 18, 20, 22, 24, 26 or 28 (HD10, BR36, BR33 sequences) in the E1 region spanning positions 192 to 319 as shown in Figure 5;
- a sequence having a homology of more than 86%, preferably more than 88%, and most preferably more than 90% homology to the amino acid sequences as represented in SEQ ID NO 148 (type 3c); BE98 in the region spanning positions 1 to 110 in the Core region as shown in Figure 5;
- a sequence having a homology of more than 76%, preferably more than 78%, most preferably more than 80% to any of the amino acid sequences as represented in SEQ ID NO 30, 32, 34, 36, 38 or 40 (HCCl53, HD10, BR36 sequences) in the region spanning positions 1646 to 1764 in the NS3/NS4 region as shown in Figure 7 and 11;
- a sequence having a homology of more than 81%, preferably more than 83%, and most preferably more than 86% homology to any of the amino acid sequences as represented in SEQ ID NO 14, 16, 18, 20, 22, 24, 26 or 28 (HD10, BR36, BR33 sequences) in the region spanning positions 140 to 319 in the Core/E1 region as shown in Figure 5;
- a sequence having a homology of more than 81.5%, preferably more than 83%, and most

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preferably more than 86% homology to any of the amino acid sequences as represented in SEQ ID NO 14, 16, 18, 20, 22, 24, 26 or 28 (HD10, BR36, BR33 sequences) in the E1 region spanning positions 192 to 319 as shown in Figure 5:

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- a sequence having a homology of more than 86%, preferably more than 88%, most preferably more than 90% to the amino acid sequence as represented in SEQ ID NO 150; (type 3c BE98) in the region spanning positions 2645 to 2757 in the NS5B region as shown in Figure 2.

According to yet another embodiment, the present invention relates to a composition as defined above, wherein said contiguous sequence is selected from any of the following HCV amino acid type 4 sequences:

- a sequence having a homology of more than 80%, preferably more than 82%, most preferably more than 84% homology to any of the amino acid sequences as represented in SEQ ID NO 118, 120, and 122 (GB358, GB549, GB809 sequences) in the region spanning positions 127 to 319 of the Core/E1 region as shown in Figure 5:
- a sequence having a homology of more than 73%, preferably more than 75%, most preferably more than 78% homology in the E1 region spanning positions 192 to 319 to any of the amino acid sequences as represented in SEQ ID NO 118, 120, and 122 (GB358, GB549, GB809 sequences) in the region spanning positions 140 to 319 of the Core/E1 region as shown in Figure 5;
- a sequence having more than 85%, preferably more than 86%, most preferably more than 87% homology to any of the amino acid sequences as represented in SEQ ID NO 118, 120 or 122 (GB358, GB549, GB809 sequences) in the region spanning positions 192 to 319 of E1 as shown in Figure 5;
- a sequence showing more than 73%, preferably more than 74%, most preferably more than 75% homology to any of the amino acid sequences as represented in SEQ ID NO 106, 108, 110, 112, 114 or 116 (GB48, GB116, GB215, GB358, GB549, GB809 sequences) in the region spanning positions 2645 to 2757 of the NS5B region as shown in Figure 2;
- a sequence having any of the sequences as represented in SEQ ID NO 164 or 166 (GB809 and CAM600 sequences) in the Core/E1 region as shown in Figure 5;
- a sequence having any of the sequences as represented in SEQ ID NO 168, 170, 172, 174,
 176, 178, 180, 182, 184, 186, 188 or 190 (CAM600, GB809, CAMG22, CAMG27,
 GB549, GB438, CAR4/1205, CAR4/901, GB116, GB215, GB958, GB809-4 sequences)
 in the E1 region as shown in Figure 5;

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a sequence having any of the sequences as represented in SEQ ID NO 192, 194, 196, 198,
 200, 202, 204, 206, 208, 210, 212 (GB358, GB724, BE100, PC, CAM600, CAMG22,
 etc.) in the NS5B region.

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The above-mentioned type 4 peptides polypeptides comprise at least an amino acid sequence selected from any HCV type 4 polyprotein with the exception of core sequence as disclosed by Simmonds et al. (1993, EG-29, see Figure 5).

According to yet another aspect, the present invention relates to a composition as defined above, wherein said contiguous sequence is selected from any of the following HCV amino acid type 5 sequences:

- a sequence having more than 93%, preferably more than 94%, most preferably more than 95% homology in the region spanning Core positions 1 to 191 to any of the amino acid sequences as represented in SEQ ID NO 42, 44, 46, 48, 50, 52 or 54 (PC sequences) and SEQ ID NO 152 (BE95) as shown in Figure 5;
 - a sequence having more than 73%, preferably more than 74%, most preferably more than 76% homology in the region spanning E1 positions 192 to 319 to any of the amino acid sequences as represented in SEQ ID NO 42, 44, 46, 48, 50, 52 or 54 (PC sequences) as shown in Figure 5;
- a sequence having a more than 78%, preferably more than 80%, most preferably more than 83% homology to any of the amino acid sequences as represented in SEQ ID NO 42, 44, 46, 48, 50, 52, 54, 154, 156 (BE95, BE100) (PC sequences) in the region spanning positions 1 to 319 of the Core/E1 region as shown in Figure 5;
- a sequence having more than 90%, preferably more than 91%, most preferably more than 92% homology to any of the amino acid sequences represented in SEQ ID NO 56 to 58 (PC sequences) in the region spanning positions 1286 to 1403 of the NS3 region as shown in Figure 7 or 11;
- a sequence having more than 66%, more particularly 68%, most particularly 70% or more homology to any of the amino acid sequences as represented in SEQ ID NO 60 or 62 (PC sequences) in the region spanning positions 1646 to 1764 of the NS3/4 region as shown in Figure 7 or 11.

According to yet another embodiment, the present invention relates to a composition as defined above, wherein said contiguous sequence is selected from any of the following HCV amino acid type 2d sequences:

- a sequence having more than 83%, preferably more than 85%, most preferably more than

- 87% homology to the amino acid sequence as represented in SEQ ID NO 144 (NE92) in the region spanning positions 1 to 319 of the Core/E1 region as shown in Figure 5;
- a sequence having more than 79%, preferably more than 81%, most preferably more than 84% homology in the region spanning E1 positions 192 to 319 to the amino acid sequence as represented in SEO ID NO 144 (NE92) as shown in Figure 12:
- a sequence having more than 95%, more particularly 96%, most particularly 97% or more homology to the amino acid sequence as represented in SEQ ID NO 146 (NE92) in the region spanning positions 2645 to 2757 of the NS5B region as shown in Figure 2.

The present invention also relates to a recombinant vector, particularly for cloning and/or expression, with said recombinant vector comprising a vector sequence, an appropriate prokaryotic, eukaryotic or viral promoter sequence followed by the nucleotide sequences as defined above, with said recombinant vector allowing the expression of any one of the HCV type 2 and/or HCV type 3 and/or type 4 and/or type 5 derived polypeptides as defined above in a prokaryotic, or eukaryotic host or in living mammals when injected as naked DNA, and more particularly a recombinant vector allowing the expression of any of the following HCV type 2d, type 3, type 4 or type 5 polypeptides spanning the following amino acid positions:

- a polypeptide starting at position 1 and ending at any position in the region between positions 70 and 326, more particularly a polypeptide spanning positions 1 to 70, 1 to 85, positions 1 to 120, positions 1 to 150, positions 1 to 191, positions 1 to 200, for expression of the Core protein, and a polypeptide spanning positions 1 to 263, positions 1 to 326, for expression of the Core and E1 protein;
- a polypeptide starting at any position in the region between positions 117 and 192, and ending at any position in the region between positions 263 and 326, for expression of E1, or forms that have the putative membrane anchor deleted (positions 264 to 293 plus or minus 8 amino acids);
- a polypeptide starting at any position in the region between positions 1556 and 1688, and ending at any position in the region between positions 1739 and 1764, for expression of the NS4 regions, more particularly a polypeptide starting at position 1658 and ending at position 1711 for expression of the NS4a antigen, and more particularly, a polypeptide starting at position 1712 and ending between positions 1743 and 1972, for example 1712-1743, 1712-1764, 1712-1782, 1712-1972, 1712 to 1782 and 1902 to 1972 for expression of the NS4b protein or parts thereof.

The term "vector" may comprise a plasmid, a cosmid, a phage, or a virus.

In order to carry out the expression of the polypeptides of the invention in bacteria such as E. coli or in eukaryotic cells such as in S. cerevisiae, or in cultured vertebrate or invertebrate hosts such as insect cells, Chinese Hamster Ovary (CHO), COS, BHK, and MDCK cells, the following steps are carried out:

transformation of an appropriate cellular host with a recombinant vector, in which a nucleotide sequence coding for one of the polypeptides of the invention has been inserted under the control of the appropriate regulatory elements, particularly a promoter recognized by the polymerases of the cellular host and, in the case of a prokaryotic host, an appropriate ribosome binding site (RBS), enabling the expression in said cellular host of said nucleotide sequence. In the case of an eukaryotic host any artificial signal sequence or pre/pro sequence might be provided, or the natural HCV signal sequence might be employed, e.g. for expression of E1 the signal sequence starting between amino acid positions 117 and 170 and ending at amino acid position 191 can be used, for expression of NS4, the signal sequence starting between amino acid positions 1646 and 1659 can be used, culture of said transformed cellular host-under conditions enabling the expression of Said insert.

The present invention also relates to a composition as defined above, wherein said polypeptide is a recombinant polypeptide expressed by means of an expression vector as defined above.

The present invention also relates to a composition as defined above, for use in a method for immunizing a mammal, preferably humans, against HCV comprising administring a sufficient amount of the composition possibly accompanied by pharmaceutically acceptable adjuvants, to produce an immune response, more particularly a vaccine composition including HCV type 3 polypeptides derived from the Core, E1 or the NS4 region and/or HCV type 4 and/or HCV type 5 polypeptides and/or HCV type 2d polypeptides.

The present invention also relates to an antibody raised upon immunization with a composition as defined above by means of a process as defined above, with said antibody being reactive with any of the polypeptides as defined above, and with said antibody being preferably a monoclonal antibody.

The monoclonal antibodies of the invention can be produced by any hybridoma liable to be formed according to classical methods from splenic cells of an animal, particularly from

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a mouse or rat, immunized against the HCV polypeptides according to the invention, or muteins thereof, or fragments thereof as defined above on the one hand, and of cells of a myeloma cell line on the other hand, and to be selected by the ability of the hybridoma to produce the monoclonal antibodies recognizing the polypeptides which has been initially used for the immunization of the animals.

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The antibodies involved in the invention can be labelled by an appropriate label of the enzymatic, fluorescent, or radioactive type.

The monoclonal antibodies according to this preferred embodiment of the invention may be humanized versions of mouse monoclonal antibodies made by means of recombinant DNA technology, departing from parts of mouse and/or human genomic DNA sequences coding for H and L chains or from cDNA clones coding for H and L chains.

Alternatively the monoclonal antibodies according to this preferred embodiment of the invention may be human monoclonal antibodies. These antibodies according to the present embodiment of the invention can also be derived from human peripheral blood lymphocytes of patients infected with type 3, type 4 or type 5 HCV, or vaccinated against HCV. Such human monoclonal antibodies are prepared, for instance, by means of human peripheral blood lymphocytes (PBL) repopulation of severe combined immune deficiency (SCID) mice (for recent review, see Duchosal et al. 1992).

The invention also relates to the use of the proteins of the invention, muteins thereof, or peptides derived therefrom for the selection of recombinant antibodies by the process of repertoire cloning (Persson et al., 1991).

Antibodies directed to peptides derived from a certaing genotype may be used either for the detection of such HCV genotypes, or as therapeutic agents.

The present invention also relates to the use of a composition as defined above for incorporation into an immunoassay for detecting HCV, present in biological sample liable to contain it, comprising at least the following steps:

- (i) contacting the biological sample to be analyzed for the presence of HCV antibodies with any of the compositions as defined above preferably in an immobilized form under appropriate conditions which allow the formation of an immune complex, wherein said polypeptide can be a biotinylated polypeptide which is covalently bound to a solid substrate by means of streptavidin or avidin complexes,
- (ii) removing unbound components,
- (iii) incubating the immune complexes formed with heterologous antibodies, which

specifically bind to the antibodies present in the sample to be analyzed, with said heterologous antibodies having conjugated to a detectable label under appropriate conditions,

(iv) detecting the presence of said immunecomplexes visually or by means of densitometry and inferring the HCV serotype present from the observed hybridization pattern.

The present invention also relates to the use of a composition as defined above, for incorporation into a serotyping assay for detecting one or more serological types of HCV present in a biological sample liable to contain it, more particularly for detecting E1 and NS4 antigens or antibodies of the different types to be detected combined in one assay format, comprising at least the following steps:

- contacting the biological sample to be analyzed for the presence of HCV antibodies
 or antigens of one or more serological types, with at least one of the compositions
 as defined above, an immobilized form under appropriate conditions which allow
 the formation of an immunecomplex,
- (ii) removing unbound components,
- (iii) incubating the immunecomplexes formed with heterologous antibodies, which specifically bind to the antibodies present in the sample to be analyzed, with said heterologous antibodies having conjugated to a detectable label under appropriate conditions.
- (iv) detecting the presence of said immunecomplexes visually or by means of densitometry and inferring the presence of one or more HCV serological types present from the observed binding pattern.

The present invention also relates to the use of a composition as defined above, for immobilization on a solid substrate and incorporation into a reversed phase hybridization assay, preferably for immobilization as parallel lines onto a solid support such as a membrane strip, for determining the presence or the genotype of HCV according to a method as defined above.

The present invention thus also relates to a kit for determining the presence of HCV genotypes as defined above present in a biological sample liable to contain them, comprising:

possibly at least one primer composition containing any primer selected from those defined above or any other HCV type 3 and/or HCV type 4, and/or HCV type 5, or universal HCV primers.

- at least one probe composition as defined above, with said probes being preferentially immobilized on a solid substrate, and more preferentially on one and the same membrane strip,
- a buffer or components necessary for producing the buffer enabling hybridization reaction between these probes and the possibly amplified products to be carried out,
- means for detecting the hybrids resulting from the preceding hybriziation,
- possibly also including an automated scanning and interpretation device for inferring the HCV genotypes present in the sample from the observed hybridization pattern.

The genotype may also be detected by means of a type-specific antibody as defined above, which is linked to any polynucleotide sequence that can afterwards be amplified by PCR to detect the immune complex formed (Immuno-PCR, Sano et al., 1992);

The present invention also relates to a kit for determining the presence of HCV antibodies as defined above present in a biological sample liable to contain them, comprising:

- at least one polypeptide composition as defined above, preferentially in combination with other polypeptides or peptides from HCV type 1, HCV type 2 or other types of HCV, with said polypeptides being preferentially immobilized on a solid substrate, and more preferentially on one and the same membrane strip,
- a buffer or components necessary for producing the buffer enabling binding reaction between these polypeptides and the antibodies against HCV present in the biological sample,
- means for detecting the immunecomplexes formed in the preceding binding reaction,
- possibly also including an automated scanning and interpretation device for inferring the HCV genotypes present in the sample from the observed binding pattern.

Figure Legends

Figure 1

Alignment of consensus nucleotide sequences for each of the type 3a isolates BR34, BR36, and BR33, deduced from the clones with SEQ ID NO 1, 5, 9; type 4 isolates GB48, GB116, GB215, GB358, GB549, GB809, CAM600, CAMG22, GB438, CAR4/1205, CAR1/501 (SEQ ID NO. 106, 108, 110, 112, 114, 116, 201, 203, 205, 207, 209 and 211); type 5a isolates BE95 and BE96 (SEQ ID NO 159 and 161) and type 2d isolate NE92 (SEQ ID NO 145) from the region between nucleotides 7932 and 8271, with known sequences from the corresponding region of isolates HCV-1, HCV-J, HC-J6, HC-J8, T1 and T9, and others as shown in Table 3.

Figure 2

Alignment of amino acids sequences deduced from the nucleic acid sequences as represented in Figure 1 from the subtype 3a clones BR34 (SEQ ID NO 2, 4), BR36 (SEQ ID NO 6, 8) and BR33 (SEQ ID NO 10, 12), the subtype 3c clone BE98 (SEQ ID NO 150), and the type 4 clones GB48 (SEQ ID NO 107), GB116 (SEQ ID NO 109), GB215 (SEQ ID NO 111), GB358 (SEQ ID NO 113), GB549 (SEQ ID NO 115) GB809 (SEQ ID NO 117); CAM600, CAMG22, GB438, CAR4/1205, CAR1/501 (SEQ ID NO 202, 204, 206, 208, 210, 212); the type 5a clones BE95 and BE96 (SEQ ID NO 160 and 162); as well as the subtype 2d isolate NE92 (SEQ ID NO 146) from the region between amino acids 2645 to 2757 with known sequences from the corresponding region of isolates HCV-I, HCV-I, HC-I6, and HC-J8, T1 and T9, and other sequences as shown in Table 3.

Figure 3

Aligment of type 2d, 3c, 4 and 5a nucleotide sequences from isolates NE92, BE98, GB358, GB809, CAM600, GB724, BE95 (SEQ ID NO 143, 147, 191, 163, 165, 193 and 151) in the Core region between nucleotide positions 1 and 500, with known sequences from the corresponding region of type 1, type 2, type 3 and type 4 sequences.

Figure 4

Alignment of nucleotide sequences for the subtype 2d isolate NE92 (SEQ ID NO 143), the type 4 isolates GB358 (SEQ ID NO 118 and 187), GB549 (SEQ ID NO 120 and 175), and

GB809-2 (SEQ ID NO 122 and 169), GB 809-4, BG116, GB215, CAM600, CAMG22, CAMG27, GB438, CAR4/1205, CAR4/901 (SEQ ID NO 189, 183, 185, 167, 171, 173, 177, 179, 181), sequences for each of the subtype 3a isolates HD10, BR36, and BR33, (SEQ ID NO 13, 15, 17 (HD10), 19, 21 (BR36) and 23, 25 or 27 (BR23) and the subtype 5a isolates BE95 and BE100 (SEQ ID NO 143 and 195) from the region between nucleotides 379 and 957, with known sequences from the corresponding region of type 1 and 2 and 3.

Figure 5

Alignment of amino acid sequences deduced from the new HCV nucleotide sequences of the Core/E1 region of isolates BR33, BR36, HD10, GB358, GB549, and GB809, PC or BE95, CAM600, and GB724 (SEQ ID NO. 14, 20, 24, 119 or 192, 121, 123 or 164, 54 or 152, 166 and 194) from the region between positions 1 and 319, with known sequences from type 1a (HCV-1), type 1b (HCV-J), type 2a (HC-JG), type 2b (HC-J8), NZL1, HCV-TR, positions 7-89 of type 3a (E-b1), and positions 8-88 of type 4a (EG-29). V-Core, variable region with type-specific features in the core protein, V1, variable region 1 of the E1 protein, V2, variable region 3 of the E1 protein, V4, variable region 4 of the E1 protein, V5, variable region 5 of the E1 protein.

Figure 6

Alignment of nucleotide sequences of isolates HCCL53, HD10 and BR36, deduced from clones with SEQ ID NO 29, 31, 33, 35, 37 and 39, from the NS3/4 region between nucleotides 4664 to 5292, with known sequences from the corresponding region of isolates HCV-1, HCV-J, HC-J6, and HC-J8, EB1, EB2, EB6 and EB7.

Figure 7

Alignment of amino acid sequences deduced from the new HCV nucleotide sequences of the NS3/NS4 region of isolate BR36 (SEQ ID NO 36, 38 and 40) and BE95 (SEQ ID NO 270). NS4-1, indicates the region that was synthesized as synthetic peptide 1 of the NS4 region, NS4-5, indicates the region that was synthesized as synthetic peptide 5 of the NS4 region; NS4-7, indicates the region that was synthesized as synthetic peptide 7 of the NS4 region.

Figure 8

Reactivity of the three LIPA-selected (Stuyver et al., 1993) type 3 sera on the Inno-LIA HCV Ab II assay (Innogenetics) (left), and on the NS4-LIA test. For the NS4-LIA test, NS4-1, NS4-5, and NS4-7 peptides were synthesized based on the type 1 (HCV-1), type 2 (HC-J6) and type 3 (BR36) prototype isolate sequences as shown in Table 4, and applied as parallel lines onto a membrane strip as indicated. 1, serum BR33, 2, serum HD10, 3, serum DKH.

Figure 9

Nucleotide sequences of Core/E1 clones obtained from the PCR fragments PC-2, PC-3, and PC-4, obtained from serum BE95 (PC-2-1 (SEQ ID NO 41), PC-2-6 (SEQ ID NO 43), PC-4-1 (SEQ ID NO 45), PC-4-6 (SEQ ID NO 47), PC-3-4 (SEQ ID NO 49), and PC-3-8 (SEQ ID NO 51)) of subtype 5a isolate BE95.

A consensus sequence is shown for the Core and E1 region of isolate BE95, presented as PC C/E1 with SEQ ID NO 53. Y, C or T, R, A or G, S, C or G.

Figure 10

Alignment of nucleotide sequences of clones with SEQ ID NO 197 and 199 (PC sequences, see also SEQ ID NO 55, 57, 59) and SEQ ID NO 35, 37 and 39 (BR36 sequences) from the NS3/4 region between nucleotides 3856 to 5292, with known sequences from the corresponding region of isolates HCV-1, HCV-J, HC-J6, and HC-J8.

Figure 11

Alignment of amino acid sequences of subtype 5a BE95 isolate PC clones with SEQ ID NO 56 and 58, from the NS3/4 region between amino acids 1286 to 1764, with known sequences from the corresponding region of isolates HCV-1, HCV-J, HC-J6, and HC-J8.

Figure 12

Alignment of amino acid sequences of subtype 5a isolate BE95 (SEQ ID NO 158) in the E1/E2 region spanning positions 328 to 546, with known sequences from the corresponding region of isolates HCV-1, HCV-J, HC-J6, HC-J8, NZL1 and HCV-TR (see Table 3).

Figure 13

Alignment of the nucleotide sequences of subtype 5a isolate BE95 (SEQ ID NO 157) in the E1/E2 region with known HCV sequences as shown in Table 3.

EXAMPLES

Example 1: The NS5b region of HCV type 3

Type 3 sera, selected by means of the INNO-LiPA HCV research kit (Stuyver et al., 1993) from a number of Brazilian blood donors, were positive in the HCV antibody ELISA (Innotest HCV Ab II; Innogenetics) and/or in the INNO-LIA HCV Ab II confirmation test (Innogenetics). Only those sera that were positive after the first round of PCR reactions (Stuyver et al., 1993) were retained for further study.

Reverse transcription and nested PCR: RNA was extracted from 50 μ l serum and subjected to cDNA synthesis as described (Stuyver et al., 1993). This cDNA was used as template for PCR, for which the total volume was increased to 50 μ l containing 10 pmoles of each primer, 3 μ l of 10x Pfu buffer 2 (Stratagene) and 2.5 U of Pfu DNA polymerase (Stratagene). The cDNA was amplified over 45 cycles consisting of 1 min 94 °C, 1 min 50 °C and 2 min 72 °C. The amplified products were separated by electrophoresis, isolated, cloned and sequenced as described (Stuyver et al., 1993).

Type 3a and 3b-specific primers in the NS5 region were selected from the published sequences (Mori et al., 1992) as follows:

for type 3a:

HCPr161(+): 5'-ACCGGAGGCCAGGAGAGTGATCTCCTCC-3' (SEQ ID NO 63) and HCPr162(-): 5'-GGGCTGCTCTATCCTCATCGACGCCATC-3' (SEO ID NO 64):

for type 3b:

HCPr163(+): 5'-GCCAGAGGCTCGGAAGGCGATCAGCGCT-3' (SEQ ID O 65) and HCPr164(-): 5'-GAGCTGCTCTGTCCTCCTCGACGCCGCA-3' (SEO ID NO 66)

Using the Line Probe Assay (LiPA) (Stuyver et al., 1993), seven high-titer type 3 sera were selected and subsequently analyzed with the primer sets HCPr161/162 for type 3a, and HCPr163/164 for type 3b. None of these sera was positive with the type 3b primers. NS5 PCR fragments obtained using the type 3a primers from serum BR36 (BR36-23), serum BR33 (BR33-2) and serum BR34 (BR34-4) were selected for cloning. The following sequences were obtained from the PCR fragments:

From fragment BR34-4:

BR34-4-20 (SEQ ID NO 1), BR34-4-19 (SEQ ID NO 3)

From fragment BR36-23:

BR36-23-18 (SEO ID NO 5), BR36-23-20 (SEO ID NO 7)

From fragment BR33-2:

BR33-2-17 (SEQ ID NO 9), BR33-2-21 (SEQ ID NO 11)

An alignment of sequences with SEQ ID NO 1, 5 and 9 with known sequences is given in Figure 1. An alignment of the deduced amino acid sequences is shown in Figure 2. The 3 isolates are very closely related to each other (mutual homologies of about 95%) and to the published sequences of type 3a (Mori et al., 1992), but are only distantly related to type 1 and type 2 sequences (Table 5). Therefore, it is clearly demonstrated that NSS sequences from LiPA-selected type 3 sera are indeed derived from a type 3 genome. Moreover, by analyzing the NSS region of serum BR34, for which no 5'UR sequences were determined as described in Stuyver et al. (1993), the excellent correlation between typing by means of the LiPA and genotyping as deduced from nucleotide sequencing was further proven.

Example 2: The Core/E1 region of HCV type 3

After aligning the sequences of HCV-1 (Choo et al., 1991), HCV-J (Kato et al., 1990), HC-J6 (Okamoto et al., 1991), and HC-J8 (Okamoto et al., 1992), PCR primers were chosen in those regions of little sequence variation. Primers HCPr23(+): 5'-CTCATGGGGTACATTCCGCT-3' (SEQ ID NO 67) and HCPr54(-): 5'-TATTACCAGTTCATCATCATCATCATCAS' (SEQ ID NO 68), were synthesized on a 392 DNA/RNA synthesizer (Applied Biosystems). This set of primers was selected to amplify the sequence from nucleotide 397 to 957 encoding amino acids 140 to 319 (Kato et al., 1990): 52 amino acids from the carboxyterminus of core and 128 amino acids of E1 (Kato et al., 1990). The amplification products BR36-9, BRR33-1, and HD10-2 were cloned as described (Stuyver et al., 1993). The following clones were obtained from the PCR fragments:

From fragment HD10-2:

HD10-2-5 (SEQ ID NO 13), HD10-2-14 (SEQ ID NO 15), HD10-2-21 (SEQ ID NO 17) From fragment BR36-9:

BR36-9-13 (SEO ID NO 19), BR36-9-20 (SEO ID NO 21),

From fragment BR33-1:

BR33-1-10 (SEQ ID NO 23), BR33-1-19 (SEQ ID NO 25), BR33-1-20 (SEQ ID NO 27),
An alignment of the type 3 E1 nucleotide sequences (HD10, BR36, BR33) with SEQ ID
NO 13, 19 and 23 with known E1 sequences is presented in Figure 4. Four variations were
detected in the E1 clones from serum HD10 and BR36, while only 2 were found in BR33.
All are silent third letter variations, with the exception of mutations at position 40 (L to P)

and 125 (M to I). The homologies of the type 3 E1 region (without core) with type 1 and 2 prototype sequences are depicted in Table 5.

In total, 8 clones covering the core/E1 region of 3 different isolates were sequenced and the E1 portion was compared with the known genotypes (Table 3) as shown in Figure 5. After computer analysis of the deduced amino acid sequence, a signal-anchor sequence at the core carboxyterminus was detected which might, through analogy with type 1b (Hijikata et al., 1991), promote cleavage before the LEWRN sequence (position 192, Fig. 5). The L-to-P mutation in one of the HD10-2 clones resides in this signal-anchor region and potentially impairs recognition by signal peptidase (computer prediction). Since no examples of such substitutions were found at this position in previously described sequences, this mutation might have resulted from reverse transcriptase or Pfu polymerase misincorporation. The 4 amino-terminal potential N-linked glycosylation sites, which are also present in HCV types la and 2, remain conserved in type 3. The N-glycosylation site in type 1b (aa 250, Kato et al., 1990) remains a unique feature of this subtype. All E1 cysteines, and the putative transmembrane region (aa 264 to 293, computer prediction) containing the aspartic acid at position 279, are conserved in all three HCV types. The following hypervariable regions can be delineated: V1 from aa 192 to 203 (numbering according to Kato et al., 1990), V2 (213-223), V3 (230-242), V4 (248-257), and V5 (294-303). Such hydrophilic regions are thought to be exposed to the host defense mechanisms. This variability might therefore have been induced by the host's immune response. Additional putative N-linked glycosylation sites in the V4 region in all type 1b isolates known today and in the V5 region of HC-J8 (type 2b) possibly further contribute to modulation of the immune response. Therefore, analysis of this region, in the present invention, for type 3 and 4 sequences has been instrumental in the delineation of epitopes that reside in the V-regions of E1, which will be critical for future vaccine and diagnostics development.

Example 3: The NS3/NS4 region of HCV Type 3

For the NS3/NS4 border region, the following sets of primers were selected in the regions of little sequence variability after aligning the sequences of HCV-1 (Choo et al., 1991), HCV-J (Kato et al., 1990), HC-J6 (Okamoto et al., 1991), and HC-J8 (Okamoto et al., 1992) (smaller case lettering is used for nucleotides added for cloning purposes):

set A:

HCPr116(+); 5'-ttttAAATACATCATGRCITGYATG-3' (SEQ ID NO 69)

- HCPr66 (-): 5'-ctattaTTGTATCCCRCTGATGAARTTCCACAT-3' (SEQ ID NO 70)
 set B:
- HCPr116(+): 5'-ttttAAATACATCATGRCITGYATG-3' (SEQ ID NO 69)
- HCPr118(-): 5'-actagtcgactaYTGIATICCRCTIATRWARTTCCACAT-3' (SEQ ID NO 71) set C:
- HCPr117(+): 5'-ttttAAATACATCGCIRCITGCATGCA-3' (SEQ ID NO 72)
- HCPr66 (-): 5'-ctattaTTGTATCCCRCTGATGAARTTCCACAT-3' (SEQ ID NO 70) set D:
- HCPr117(+): 5'-ttttAAATACATCGCIRCITGCATGCA-3' (SEQ ID NO 72)
- HCPr118(-): 5'-actagtcgactaYTGIATICCRCTIATRWARTTCCACAT-3' (SEQID NO 71) set E:
- HCPr116(+): 5'-ttttAAATACATCATGRCITGYATG-3' (SEQ ID NO 69)
- HCPr119(-): actagtcgactaRTTIGCIATIAGCCG/TRTTCATCCAYTG-3' (SEQ ID NO 73) set F:
- HCPr117(+): 5'-ttttAAATACATCGCIRCITGCATGCA-3' (SEQ ID NO 72)
- HCPr119(-): actagtcgactaRTTIGCIATIAGCCG/TRTTCATCCAYTG-3' (SEQ ID NO 73) set G:
- HCPr131(+): 5'-ggaattctagaCCITCITGGGAYGARAYITGGAARTG-3' (SEO ID NO 74)
- HCPr66 (-): 5'-ctattaTTGTATCCCRCTGATGAARTTCCACAT-3' (SEQ ID NO 70) set H:
- HCPr130(+): 5'-ggaattctagACIGCITAYCARGCIACIGTITGYGC-3' (SEQ ID NO 75)
- HCPr66 (-): 5'-ctattaTTGTATCCCRCTGATGAARTTCCACAT-3' (SEQ ID NO 70)
 - set I:
- HCPr134(+): 5'-CATATAGATGCCCACTTCCTATC-3' (SEO ID NO 76)
- HCPr66 (-): 5'-ctattaTTGTATCCCRCTGATGAARTTCCACAT-3' (SEQ ID NO 70)
 - set J:
- $HCPr131(+): 5'-ggaattctagaCCITCITGGGAYGARAYITGGAARTG-3' (SEQ\ ID\ NO\ 74)$
- HCPr118(-): 5'-actagtcgactaYTGIATICCRCTIATRWARTTCCACAT-3' (SEQ ID NO 71)
 - set K:
 - $HCPr130(+);\ 5\text{'-}ggaattctagACIGCITAYCARGCIACIGTITGYGC-3'}\ (SEQ\ ID\ NO\ 75)$
- HCPr118(-): 5'-actagtcgactaYTGIATICCRCTIATRWARTTCCACAT-3' (SEQ ID NO 71)

set L:

HCPr134(+): 5'-CATATAGATGCCCACTTCCTATC-3' (SEQ ID NO 76)

HCPr118(-): 5'-actagtcgactaYTGIATICCRCTIATRWARTTCCACAT-3' (SEQID NO71)
set M:

HCPr3(+): 5'-GTGTGCCAGGACCATC-3' (SEQ ID NO 77) and

HCPr4(-): 5'-GACATGCATGTCATGATGTA-3 (SEQ ID NO 78)

set N:

HCPr3(+): 5'-GTGTGCCAGGACCATC-3' (SEQ ID NO 77) and

HCPr118(-): 5'-actagtcgactaYTGIATICCRCTIATRWARTTCCACAT-3' (SEQID NO 71) set O:

HCPr3(+): 5'-GTGTGCCAGGACCATC-3' (SEQ ID NO 77) and

HCPr66 (-): 5'-ctattaTTGTATCCCRCTGATGAARTTCCACAT-3' (SEQ ID NO 70)

No PCR products could be obtained with the sets of primers A, B, C, D, E, F, G, H, I, J, K, L, M, and N, on random-primed cDNA obtained from type 3 sera. With the primer set O, no fragment could be amplified from type 3 sera. However, a smear containing a few weakly stainable bands was obtained from serum BR36. After sequence analysis of several DNA fragments, purified and cloned from the area around 300 bp on the agarose gel, only one clone, HCCl53 (SEQ ID NO 29), was shown to contain HCV information. This sequence was used to design primer HCPr152.

A new primer set P was subsequently tested on several sera.

set P:

HCPr152(+): 5'-TACGCCTCTTCTATATCGGTTGGGGCCTG-3' (SEQ ID NO 79) and

HCPr66(-): 5'-CTATTATTGTATCCCRCTGATGAARTTCCACAT-3' (SEQ ID NO 70)

The 464-bp HCPr152/66 fragment was obtained from serum BR36 (BR36-20) and serum

HD10 (HD10-1). The following clones were obtained from these PCR products:

From fragment HD10-1:

HD10-1-25 (SEO ID NO 31), HD10-1-3 (SEO ID NO 33),

From fragment BR36-20:

BR36-20-164 (SEQ ID NO 35), BR36-20-165 (SEQ ID NO 37), BR36-20-166 (SEQ ID NO 39).

The nucleotide sequences obtained from clones with SEQ ID NO 29, 31, 33, 35, 37 or 39 are shown aligned with the sequences of prototype isolates of other types of HCV in Figure 6. In addition to one silent 3rd letter variation, one 2nd letter mutation resulted in an

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E to G substitution at position 175 of the deduced amino acid sequence of BR36 (Fig. 7). Serum HD10 clones were completely identical. The two type 3 isolates were nearly 94% homologous in this NS4 region. The homologies with other types are presented in Table 5.

Example 4: Analysis of the anti-NS4 response to type-specific peptides

As the NS4 sequence contains the information for an important epitope cluster, and since antibodies towards this region seem to exhibit little cross-reactivity (Chan et al., 1991), it was worthwhile to investigate the type-specific antibody response to this region. For each of the 3 genotypes, HCV-1 (Choo et al., 1991), HC-J6 (Okamoto et al., 1991) and BR36 (present invention), three 20-mer peptides were synthesized covering the epitope region between amino acids 1688 and 1743 (as depicted in table 6). The synthetic peptides were applied as parallel lines onto membrane strips. Detection of anti-NS4 antibodies and color development was performed according to the procedure described for the INNO-LIA HCV Ab II kit (Innogenetics, Antwerp). Peptide synthesis was carried out on a 9050 PepSynthesizer (Millipore). After incubation with 15 LiPA-selected type 3 sera, 9 samples showed reactivity towards NS4 peptides of at least 2 different types, but a clearly positive reaction was observed for 3 sera (serum BR33, HD30 and DKH) on the type 3 peptides, while negative (serum BR33 and HD30) or indeterminate (serum DKH) on the type 1 and type 2 NS4 peptides; 3 sera tested negative for anti-NS4 antibodies (Figure 8). Using the same membrane strips coated with the 9 peptides as indicated above and as shown in Figure 8, 38 type 1 sera (10 type 1a and 28 type 1b), 11 type 2 sera (10 type 2a and 1 type 2b), 12 type 3a sera and 2 type 4 sera (as determined by the LiPA procedure) were also tested. As shown in Table 8. the sera reacted in a genotype-specific manner with the NS4 epitopes. These results demonstrate that type-specific anti-NS4 antibodies can be detected in the sera of some patients. Such genotype-specific synthetic peptides might be employed to develop serotyping assays, for example a mixture of the nine peptides as indicated above, or combined with the NS4 peptides from the HCV type 4 or 6 genotype or from new genotypes corresponding to the region between amino acids 1688 and 1743, or synthetic peptides of the NS4 region between amino acids 1688 and 1743 of at least one of the 6 genotypes, combined with the E1 protein or deletion mutants thereof, or synthetic E1 peptides of at least one of the genotypes. Such compositions could be further extended with type-specific peptides or proteins, including for example the region between amino acids 68 and 91 of the core protein, or more preferably the region between amino acids 68 and 78. Furthermore, such type-specific

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55 antigens may be advantageously used to improve current diagnostic screening and confirmation assays and/or HCV vaccines.

Example 5 The Core and E1 regions of HCV type 5

Sample BE95 was selected from a group of sera that reacted positive in a prototype Line Probe Assay as described earlier (Stuyver et al., 1993), because a high-titer of HCV RNA could be detected, enabling cloning of fragments by a single round of PCR. As no sequences from any coding region of type 5 has been disclosed yet, synthetic oligonucleotides for PCR amplification were chosen in the regions of little sequence variation after aligning the sequences of HCV-1 (Choo et al., 1991), HCV-J (Kato et al., 1990), HC-J6 (Okamoto et al., 1991). HC-J8 (Okamoto et al., 1992), and the new type 3 sequences of the present invention HD10, BR33, and BR36 (see Figure 5, Example 2). The following sets of primers were synthesized on a 392 DNA/RNA synthesizer (Applied Biosystems):

Set 1:

HCPr52(+): 5'-atgTTGGGTAAGGTCATCGATACCCT-3' (SEQ ID NO 80) and HCPr54(-): 5'-ctattaCCAGTTCATCATCATATCCCA-3' (SEO ID NO 78) Set 2:

HCPr41(+): 5'-CCCGGGAGGTCTCGTAGACCGTGCA-3' (SEO ID NO 81) and HCPr40(-): 5'-ctattaAAGATAGAGAAAGAGCAACCGGG-3'(SEO ID NO 82) Set 3:

HCPr41(+): 5'-CCCGGGAGGTCTCGTAGACCGTGCA-3' (SEO ID NO 81) and HCPr54(-): 5'-ccattaCCAGTTCATCATCATATCCCA-3' (SEQ ID NO 78)

The three sets of primers were employed to amplify the regions of the type 5 isolate PC as described (Stuyver et al., 1993). Set 1 was used to amplify the E1 region and vielded fragment PC-4, set 2 was designed to yield the Core region and yielded fragment PC-2. Set 3 was used to amplify the Core and E1 region and yielded fragment PC-3. These fragments were cloned as described (Stuyver et al., 1993). The following clones were obtained from the PCR fragments:

From fragment PC-2:

PC-2-1 (SEQ ID NO 41), PC-2-6 (SEQ ID NO 43),

From fragment PC-4:

PC-4-1 (SEO ID NO 45), PC-4-6 (SEO ID NO 47),

From fragment PC-3:

PC-3-4 (SEO ID NO 49), PC-3-8 (SEO ID NO 51)

An alignment of sequences with SEQ ID NO 41, 43, 45, 47, 49 and 51, is given in Figure 9. A consensus amino acid sequence (PC C/E1; SEQ ID NO 54) can be deduced from each of the 2 clones cloned from each of the three PCR fragments as depicted in Figure 5, which overlaps the region between nucleotides 1 and 957 (Kato et al., 1990). The 6 clones are very closely related to each other (mutual homologies of about 99.7%).

An alignment of nucleotide sequence with SEQ ID NO 53 or 151 (PC C/E1 from isolate BE95) with known nucleotide sequences from the Core/E1 region is given in Figure 3. The clone is only distantly related to type 1, type 2, type 3 and type 4 sequences (Table 5).

Example 6: NS3/NS4 region of HCV type 5

Attempts were undertaken to clone the NS3/NS4 region of the isolate BE95, described in example 5. The folllowing sets of primers were selected in the regions of little sequence variability after aligning the sequences of HCV-1 (Choo et al., 1991), HCV-J (Kato et al., 1991), HC-J6 (Okamoto et al., 1991), and HC-J8 (Okamoto et al., 1992) and of the sequences obtained from type 3 sera of the present invention (SEQ ID NO 31, 33, 35, 37 and 39); smaller case lettering is used for nucleotides added for cloning purposes:

set A:

HCPr116(+): 5'-ttttAAATACATCATGRCITGYATG-3' (SEO ID NO 66)

HCPr66 (-): 5'-ctattaTTGTATCCCRCTGATGAARTTCCACAT-3' (SEQ ID NO 70)

set B:

HCPr116(+): 5'-ttttAAATACATCATGRCITGYATG-3' (SEQ ID NO 69)

HCPr118(-): 5'-actagtegactaYTGIATICCRCTIATRWARTTCCACAT-3' (SEQ ID NO 71) set C:

HCPr117(+): 5'-ttttAAATACATCGCIRCITGCATGCA-3' (SEQ ID NO 72)

HCPr66 (-): 5'-ctattaTTGTATCCCRCTGATGAARTTCCACAT-3' (SEQ ID NO 70)
set D:

HCPr117(+): 5'-ttttAAATACATCGCIRCITGCATGCA-3' (SEQ ID NO 72)

 $HCPr118(-): 5"-actagtcgactaYTGIATICCRCTIATRWARTTCCACAT-3" (SEQ\,ID\,NO\,71)$

set E:

HCPr116(+): 5'-ttttAAATACATCATGRCITGYATG-3' (SEO ID NO 69)

HCPr119(-): actagtcgactaRTTIGCIATIAGCCG/TRTTCATCCAYTG-3' (SEQ ID NO 73)

set F:

- HCPr117(+): 5'-ttttAAATACATCGCIRCITGCATGCA-3' (SEQ ID NO 72)
- HCPr119(-); actagtcgactaRTTIGCIATIAGCCG/TRTTCATCCAYTG-3' (SEQ ID NO 73) set G:
- HCPr131(+): 5'-ggaattctagaCCITCITGGGAYGARAYITGGAARTG-3' (SEQ ID NO 74)
- HCPr66 (-): 5'-ctattaTTGTATCCCRCTGATGAARTTCCACAT-3' (SEQ ID NO 70) set H:
- HCPr130(+): 5'-ggaattctagACIGCITAYCARGCIACIGTITGYGC-3' (SEQ ID NO 75)
- HCPr66 (-): 5'-ctattaTTGTATCCCRCTGATGAARTTCCACAT-3' (SEQ ID NO 70)
 - set I:
- HCPr134(+): 5'-CATATAGATGCCCACTTCCTATC-3' (SEQ ID NO 76)
- HCPr66 (-): 5'-ctattaTTGTATCCCRCTGATGAARTTCCACAT-3' (SEQ ID NO 70) set J:
- HCPr131(+): 5'-ggaattctagaCCITCITGGGAYGARAYITGGAARTG-3' (SEQ ID 74)
- HCPr118(-): 5'-actagtcgactaYTGIATICCRCTIATRWARTTCCACAT-3' (SEQID NO71)
 set K'-
- HCPr130(+): 5'-ggaattctagACIGCITAYCARGCIACIGTITGYGC-3' (SEQ ID NO 75)
- HCPr118(-): 5'-actagtogactaYTGIATICCRCTIATRWARTTCCACAT-3' (SEQID NO 71) set L:
- HCPr134(+): 5'-CATATAGATGCCCACTTCCTATC-3' (SEO ID NO 76)
- HCPr118(-): 5'-actagtcgactaYTGIATICCRCTIATRWARTTCCACAT-3' (SEQID NO71) set M:
- HCPr3(+): 5'-GTGTGCCAGGACCATC-3' (SEQ ID NO 77) and
- HCPr4(-): 5'-GACATGCATGTCATGATGTA-3' (SEQ ID NO 78)
 - set N:
- HCPr3(+): 5'-GTGTGCCAGGACCATC-3' (SEO ID NO 77) and
- HCPr118(-): 5'-actagtegactaYTGIATICCRCTIATRWARTTCCACAT-3' (SEQ ID NO 7i)
 - set O:
 - HCPr3(+): 5'-GTGTGCCAGGACCATC-3' (SEQ ID NO 77) and
 - HCPr66 (-): 5'-ctattaTTGTATCCCRCTGATGAARTTCCACAT-3' (SEQ ID NO 70)
 - No PCR products could be obtained with the sets of primers A, B, C, D, E, F, G, H, I, J, K, L, M, and N, on random-primed cDNA obtained from type 3 sera. However,

set O yielded what appeared to be a PCR artifact fragment estimated about 1450 base pairs, instead of the expected 628 base pairs. Although it is not expected that PCR artifact fragments contain information of the gene or genome that was targetted in the experiment, efforts were put in cloning of this artifact fragment, which was designated fragment PC-1. The following clones, were obtained from fragment PC-1:

PC-1-37 (SEQ ID NO 59 and SEQ ID NO 55), PC-1-48 (SEQ ID NO 61 and SEQ ID NO 57)

The sequences obtained from the 5' and 3' ends of the clones are given in SEQ ID NOS 55, 57, 59, and 61, and the complete sequences with SEQ ID NO 197 and 199 are shown aligned with the sequences of prototype isolates of other types of HCV in Figure 10 and the alignment of the deduced amino acid sequences is shown in Figure 11 and 7. Surprisingly, the PCR artifact clone contained HCV information. The positions of the sequences within the HCV genome are compatible with a contiguous HCV sequence of 1437 nucleotides, which was the estimated size of the cloned PCR artifact fragment. Primer HCPr66 primed correctly at the expected position in the HCV genome. Therefore, primer HCPr3 must have incidentally misprimed at a position 809 nucleotides upstream of its legitimate position in the HCV genome. This could not be expected since no sequence information was available from a coding region of type 5.

Example 7: The E2 region of HCV type 5

Serum BE95 was chosen for experiments aimed at amplifying a part of the E2 region of HCV type 5.

After aligning the sequences of HCV-1 (2), HCV-J(1), HC-J6 (3), and HC-J8 (4), PCR primers were chosen in those regions of little sequence variation.

Primers HCPr109(+): 5'-TGGGATATGATGATGAACTGGTC-3' (SEQ ID NO 141) and HCPr14(-): 5'-CCAGGTACAACCGAACCAATTGCC-3' (SEQ ID NO 142) were combined to amplify the aminoterminal region of the E2/NS1 region, and were synthesized on a 392 DNA/RNA synthesizer (Applied Biosystems). With primers HCPr109 and HCPr14, a PCR fragment of 661 bp was generated, containing 169 nucleodtides corresponding to the E1 carboxyterminus and 492 bases from the region encoding the E2 aminoterminus.

An alignment of the type 5 E1/E2 sequences with seq ID NO. 158 with known sequences is presented in Figure 10. The deduced protein sequence was compared with the different

genotypes (Fig. 12, amino acids 328-546). In the E1 region, there were no extra structural important motifs found. The aminoterminal part of E2 was hypervariable when compared with the other genotypes. All 6 N-glycosylation sites and all 7 cysteine residue's were conserved in this E2 region. To preserve alignment, it was necessary to introduce a gap between aa 474 and 475 as for type 3a, but not between aa 480 and 481, as for type 2.

Example 8: The NS5b region of HCV type 4

Type 4 sera GB48, GB116, GB215, and GB358, selected by means of the line probe assay (LiPA, Stuyver et al., 1993), as well as sera GB549 and GB809 that could not be typed by means of this LiPA (only hybridization was observed with the universal probes), were selected from Gabonese patients. All these sera were positive after the first round of PCR reactions for the 5' untranslated region (Stuyver et al., 1993) and were retained for further study.

RNA was isolated from the sera and cDNA synthesized as described in example 1.

Universal primers in the NS5 region were selected after alignment of the published sequences as follows:

HCPr206(+): 5'-TGGGGATCCCGTATGATACCCGCTGCTTTGA-3'

(SEQ ID NO. 124) and

HCPr207(-): 5'-GGCGGAATTCCTGGTCATAGCCTCCGTGAA-3'

(SEO ID NO. 125):

and were synthesized on a 392 DNA/RNA synthesizer (Applied Biosystems). Using the Line Probe Assay (LiPA), four high-titer type 4 sera and 2 sera that could not be classified were selected and subsequently analyzed with the primer set HCPr206/207. NS5 PCR fragments obtained using these primers from serum GB48 (GB48-3), serum GB116 (GB116-3), serum GB215 (GB215-3), serum GB358 (GB358-3), serum GB549 (GB549-3), and serum GB809 (GB809-3), were selected for cloning. The following sequences were obtained from the PCR fragments:

From fragment GB48-3: GB48-3-10 (SEQ ID NO. 106)

From fragment GB116-3: GB116-3-5 (SEQ ID NO. 108)

From fragment GB215-3: GB215-3-8 (SEQ ID NO. 110)

From fragment GB358-3: GB358-3-3 (SEQ ID NO. 112)

From fragment GB549-3: GB549-3-6 (SEQ ID NO. 114)

From fragment GB809-3: GB809-3-1 (SEO ID NO. 116)

An alignment of nucleotide sequences with SEQ ID NO. 106, 108, 110, 112, 114, and 116 with known sequences is given in Figure 1. An alignment of deduced amino acid sequences with SEQ ID NO. 107, 109, 111, 113, 115, and 117 with known sequences is given in Figure 2. The 4 isolates that had been typed as type 4 by means of LiPA are very closely related to each other (mutual homologies of about 95%), but are only distantly related to type 1, type 2, and type 3 sequences (e.g. GB358 shows homologies of 65.6 to 67.7% with other genotypes, Table 4). The sequence obtained from sera GB549 and GB809 also show similar homologies with genotypes 1, 2, and 3 (65.9 to 68.8% for GB549 and 65.0 to 68.5% for GB809. Table 4), but an intermediate homology of 79.7 to 86.8% (often observed between subtypes of the same type) exists between GB549 or GB809 with the group of isolates consisting of GB48, GB116, GB215, and GB358, or between GB549 and GB809. These data indicate the discovery of 3 new subtypes within the HCV genotype 4: in the present invention, these 3 subtypes are designated subtype 4c, represented by isolates GB48, GB116. GB215, and GB358, subtype 4g, represented by isolate GB549, and subtype 4e, represented by isolate GB809. Although the homologies observed between subtypes in the NS5 region seem to indicate a closer relationship between subtypes 4c and 4e, the homologies observed in the E1 region indicate that subtypes 4g and 4e show the closest relation (see example 8).

Example 9: The Core/E1 region of HCV type 4

From each of the 3 new type 4 subtypes, one representative serum was selected for cloning experiments in the Core/E1 region. GB549 (subtype 4g) and GB809 (subtype 4e) were analyzed together with isolate GB358 that was chosen from the subtype 4c group. Synthetic oligonucleotides:

After aligning the sequences of HCV-1 (2), HCV-J(1), HC-J6 (3), and HC-J8 (4), PCR primers were chosen in those regions of little sequence variation.

Primers HCPr52(+): 5'-atgTTGGGTAAGGTCATCGATACCCT-3', HCPr23(+): 5'-CTCATTGGTACCATTGATACCCT-3', and HCPr54(-): 5'-CTATTACCAGTTCATCATCATATCCCA-3', were synthesized on a 392 DNA/RNA synthesizer (Applied Biosystems). The sets of primers HCPr23/54 and HCPr52/54 were used, but only with the primer set HCPr52/54, PCR fragments could be obtained. This set of primers amplified the sequence from nucleotide 379 to 957 encoding amino acids 127 to 319: 65 amino acids from the carboxyterminus of core and 128 amino acids of E1. The

amplification products GB358-4, GB549-4, and GB809-4 were cloned as described in example

1. The following clones were obtained from the PCR fragments:

From fragment GB358-4: GB358-4-1 (SEO ID NO 118)

From fragment GB549-4: GB549-4-3 (SEO ID NO 120)

From fragment GB809-4: GB809-4-3 (SEQ ID NO 122)

An alignment of the type 4 Core/E1 nucleotide sequences with seq ID NO. 118, 120, and 122 with known sequences is presented in Figure 4. The homologies of the type 4 E1 region (without core) with type 1, type 2, type 3, and type 5 prototype sequences are depicted in Table 4. Homologies of 53 to 66% are observed with representative isolates of non-type 4 genotypes. Observed homologies in the E1 region within type 4, between the different subtypes, ranges from 75.2 to 78.4%. The recently disclosed sequences of the core region of Egyptian type 4 isolates (for example EG-29 in Figure 3) described by Simmonds et al. (1993) do not allow alignment with the Gabonese sequences (as described in the present invention) in the NSB region and may belong to different type 4 subtypes(s) as can be deduced from the core sequences. The deduced amino acid sequences with SEQ ID NO 119, 121, and 123 are aligned with other prototype sequences in Figure 5. Again, type-specific variation mainly resides in the variable V regions, designated in the present invention, and therefore, type-4-specific amino acids or V regions will be instrumental in diagnosis and therapeutics for HCV type 4.

Example 10: The Core/E1 and NS5b regions of new HCV type 2, 3 and 4 subtypes

Samples NE92 (subtype 2d), BE98 (subtype 3c), CAM600 and GB809 (subtype 4e), CAMG22 and CAMG27 (subtype 4f), GB438 (subtype 4h), CAR4/1205 subtype (4i), CAR1/501 (subtype 4j), CAR1/901 (subtype 47), and GB724 (subtype 47) were selected from a group of sera that reacted positive but aberrantly in a prototype Line Probe Assay as described earlier (Stuyver et al., 1993). Another type 5a isolate BE100 was also analyzed in the C/E1 region, and yet another type 5a isolate BE96 in the NS5b region. A high-titer of HCV RNA could be detected, enabling cloning of fragments by a single round of PCR. As no sequences from any coding region of these subtypes had been disclosed yet, synthetic oligonucleotides for PCR amplification were chosen in the regions of little sequence variation after aligning the sequences of HCV-1 (Choo et al., 1991), HCV-J(Kato et al., 1990), HC-J6 (Okamoto et al., 1991), HC-J8 (Okamoto et al., 1992), and the other new sequences of the present invention.

The above mentioned sets 1, 2 and 3 (see example 5) of primers were used, but only with set 1, PCR fragments could be obtained from all isolates (except for BE98, GB724, and CAR1/501). This set of primers amplified the sequence from nucleotide 379 to 957 encoding amino acids 127 to 319: 65 amino acids from the carboxyterminus of core and 128 amino acids of E1. With set 3, the core/E1 region from isolate NE92 and BE98 could be amplified, and with set 2, the core region of GB358, GB724, GB809, and CAM600 could be amplified. The amplification products were cloned as described in example 1. The following clones were obtained from the PCR fragments:

From isolate GB724, the clone with SEQ ID NO 193 from the core region.

From isolate NE92, the clone with SEQ ID NO 143

From isolate BE98, the clone from the core/E1 region of which part of the sequence has been analyzed and is given in SEO ID NO 147,

From isolate CAM600, the clone with SEQ ID NO 167 from the E1 region, or SEQ ID NO 165 from the Core/E1 region as shown in Figure 3,

From isolate CAMG22, the clone with SEQ ID NO 171 from the E1 region as shown in Figure 4.

from isolate GB358, the clone with SEQ ID NO 191 in the core region,.

from isolate CAMG27, the clone with SEQ ID NO 173 from the core/E1 region,

from isolate GB438, the clone with SEQ ID NO 177 from the core/ E1 region,

from isolate CAR4/1205, the clone with SEQ ID NO 179 from the core/E1 region,

from isolate CAR1/901, the clone with SEQ ID NO 181 from the core/ E1 region,

from isolate GB809, the clone GB809-4 with SEQ ID NO 189 from the core/E1 region,

clone GB809-2 with SEQ ID NO 169 from the core/E1 region and the clone with SEQ ID NO 163 from the core region.

and from isolate BE100, the clone with SEQ ID NO 155 from the Core/E1 region as shown in Figure 4.

An alignment of these Core/E1 sequences with known Core/E1 sequences is presented in Figure 4. The deduced amino acid sequences with SEQ ID NO 144, 148, 164, 168, 170, 172, 174, 178, 180, 182, 190, 192, 194, 156, 166 are aligned with other prototype sequences in Figure 5. Again, type-specific variation mainly resides in the variable V regions, designated in the present invention, and therefore, type 2d, 3c and type 4-specific amino acids or V regions will be instrumental in diagnosis and therapeutics for HCV type (subtype) 2d, 3c or the different type 4 subtypes.

The NS5b region of isolates NE92, BE98, CAM600, CAMG22, GB438, CAR4/1205, CAR1/501, and BE96 was amplified with primers HCPr206 and HCPr207 (Table 7). The corresponding clones were cloned and sequenced as in example 1 and the corresponding sequences (of which BE98 was partly sequenced) received the following identification numbers:

NE92: SEO ID NO 145

BE98: SEQ ID NO 149

CAM600: SEQ ID NO 201

CAMG22: SEQ ID NO 203

GB438: SEQ ID NO 207 CAR4/1205: SEQ ID NO 209

CAR1/501: SEQ ID NO 211

BE95: SEQ ID NO 159

BE96: SEO ID NO 161

An alignment of these NS5b sequences with known NS5b sequences is presented in Figure 1. The deduced amino acid sequences with SEQ ID NO 146, 150, 202, 204, 206, 208, 210, 212, 160, 162 are aligned with other prototype sequences in Figure 2. Again, subtype-specific variations can be observed, and therefore, type 2d, 3c and type 4-specific amino acids or V regions will be instrumental in diagnosis and therapeutics for HCV type (subtype) 2d, 3c or the different type 4 subtypes.

Example 11: Genotype-specific reactivity of anti-E1 antibodies (Serotyping)

El proteins were expressed from vaccinia virus constructs containing a core/El region extending from nucleotide positions 355 to 978 (Core/El clones described in previous examples including the primers HCPr52 and HCPr54), and expressed proteins from L119 (after the initiator methionine) to W326 of the HCV polyprotein. The expressed protein was modified upon expression in the appropriate host cells (e.g. HeLa, RK13, HuTK-, HepG2) by cleavage between amino acids 191 and 192 of the HCV polyprotein and by the addition of high-mannose type carbohydrate motifs. Therefore, a 30 to 32 kDa glycoprotein could be observed on western blot by means of detection with serum from patients with hepatitis C.

As a reference, a genotype 1b clone obtained form the isolate HCV-B was also expressed in an identical way as described above, and was expressed from recombinant vaccinia virus vvHCV-11A.

A panel of 104 genotyped sera was first tested for reactivity with a cell lysate containing type 1b protein expressed from the recombinant vaccinia virus vvHCV-11A, and compared with cell lysate of RK13 cells infected with a wild type vaccinia virus ("E1/WT"). The lysates were coated as a 1/20 dilution on a normal ELISA microtiter plate (Nunc maxisorb) and left to react with a 1/20 dilution of the respective sera. The panel consisted of 14 type 1a, 38 type 1b, 21 type 2, 21 type 3a, and 9 type 4 sera. Human antibodies were subsequently detected by a goat anti-human IgG conjugated with peroxidase and the enzyme activity was detected. The optical density values of the E1 and wild type lysates were divided and a factor 2 was taken as the cut-off. The results are given in the table A. Eleven out of 14 type 1a sera (79%), 25 out of 38 type 1b sera (66%), 6 out of 21 (29%), 5 out of 21 (24%), and none of the 9 type 4 or the type 5 serum reacted (0%). These experiments clearly show the high prevalence of anti-E1 antibodies reactive with the type 1 E1 protein in patients infected with type 1 (36/52 (69%)) (either type 1a or type 1b), but the low prevalence or absence in non-type 1 sera (11/52 (21%)).

TABLE A

serum	E1/WT			
type 1a				
3748	3.15			
3807	3.51			
5282	1.99			
9321	3.12			
9324	2.76			
9325	6.12			
9326	10.56			
9356	1.79			
9388	3.5			
8366	10.72			
8380	2.27			
10925	4.02			
10936	5.04			
10938	1.36			

type 1b	
5205	2.25
5222	1.33
5246	1.24
5250	13.58
5493	0.87
5573	1.75
8243	1.77
8244	2.05
8316	1.21
8358	5.04
9337	14.47
9410	5
9413	5.51
10905	1.26
10919	5.00
10928	8.72
10929	8.26
10931	2.3
10932	4.41
44	2.37
45	3.14
46	4.37
47 48	5.68 2.97
48	1.18
50	9.85
51	4.51
52	1.11
53	5.20
54	0.00
55	1.48
56	1.06
57	3.85
58	7.6
59	3.28
60	3.23
61	7.82
62	1.92

type 2	
23 24 25 26 27 28 29 30 31 32 33 34 35 36 37 38 39 40 41 42	0.91 1.16 2.51 0.96 1.20 0.96 1.20 0.92 2.58 8.05 0.92 0.82 5.75 0.79 0.85 0.76 0.92 1.08 2.33 2.83
type 3	0.91
1 2 3 4 5 6 7 8 8 9 10 11 12 13 14 15 16 17 18 19 20 21	6.88 1.47 3.06 6.52 10.24 2.72 1.11 1.54 1.60 1.21 1.07 1.00 0.85 0.96 0.51 1.00 1.09 1.04

type 4		
22	0.87	
GB48	0.49	
GB113	0.68	
GB116	0.73	
GB215	0.52	
GB358	0.56	1
GB359	0.71	ı
GB438	1.08	ı
GB516	1.04	
type 5		
BE95	0.86	

Core/E1 clones of isolates BR36 (type 3a) and BE95 (type 5a) were subsequently recombined into the viruses vvHCV-62 and vvHCV-63, respectively. A genotyped panel of sera was subsequently tested onto cell lysates obtained from RK13 cells infected with the recombinant viruses vvHCV-62 and vvHCV-63. Tests were carried out as described above and the results are given in the table given below (TABLE B). From these results, it can clearly be seen that, although some cross-reactivity occurs (especially between type 1 and 3), the obtained values of a given serum are usually higher on its homologous E1 protein than on an E1 protein of another genotype. For type 5 sera, none of the 5 sera were reactive on type 1 or 3 E1 proteins, while 3 out of 5 were shown to contain anti-E1 antibodies when tested on their homologous type 5 protein. Therefore, in this simple test system, a considerable number of sera can already be serotyped. Combined with the reactivity to type-specific NS4 epitopes or epitopes derived from other type-specific parts of the HCV polyprotein, a serotyping assay may be developed for discriminating the major types of HCV. To overcome the problem of cross-reactivity, the position of cross-reactive epitopes may be determined by someone skilled in the art (e.g. by means of competition of the reactivity with synthetic peptides), and the epitopes evoking cross-reactivity may be left out of the composition to be included in the serotyping assay or may be included in sample diluent to outcompete cross-reactive antibodies.

TABLE B

serum	E11b/WT	E13a/WT	E15a/WT		
type 1b					
8316	0.89	0.59	0.80		
8358	2.22	2.65	1.96		
9337	1.59	0.96	0.93		
9410	16.32	9.60	3.62		
9413	9.89	2.91	2.85		
10905	1.04	0.96	1.05		
10919	3.17	2.56	2.96		
10928	4.39	2.28	2.07		
10929	2.95	2.07	2.08		
10929	3.11	1.49	2.06		
5	0.86	0.86	0.96		
6	3.48	1.32	1.32		
7	6.76	4.00	3.77		
8	10.88	3.44	4.04		
9	1.76	1.88	1.58		
10	9.88	7.48	7.20		
11	8.48	8.99	8.45		
12	0.76	0.72	0.76		
13	5.04	5.67	5.37		
14	10.48	10.54	11.22		
15	5.18	1.62	1.65		
type 3					
8332	3.39	4.22	0.66		
10907	3.24	4.39	0.96		
10908	0.99	0.94	0.98		
10934	0.86	0.90	0.90		
10927	2.58	2.71	2.44		
8210	0.82	0.80	0.86		
8344	1.09	6.66	1.17		
8351	1.21	1.29	1.22		
30	0.85	4.11	0.98		
32	0.85	2.16	1.04		
type 5					
No. 200 de	0.78	0.95	1.54		
BE110	0.79	1.01	4.95		
BE95_	0.47	0.52	0.65		
BE111	0.71	0.75	8.33		
BE112	1.01	1.27	2.37		
BE113	1.11	1.35	1.60		

Table 5. Homologies of new HCV sequences with other known HCV types

Region (nucleotides)	lsolate (type)	la HCV-1	1b HCV-J	2a HC-J6	2ь НС-J8	Tl	3a T7	T9	ъ Т10
Core (1-573)	PC (5)	83.8 (91.6)	84.8 (92.1)	82.6 (90.1)	82.4 (89.0)				
El (574-957)	HD10 (3) BR36 (3) BR33 (3) PC (5) GB358 (4a) GB549 (4b) GB809 (4c)	61.5 (68.0) 62.0 (66.4) 60.7 (67.2) 61.4 (64.0) 62.5 (69.1) 66.0 (72.2) 63.3 (69.1)	64.6 (68.8) 62.5 (67.2) 63.3 (68.0) 62.4 (64.8) 62.8 (65.9) 62.8 (69.8) 60.7 (64.3)	57.8 (55.5) 56.5 (53.9) 56.5 (54.7) 54.1 (49.6) 59.4 (54.0) 59.1 (56.4) 56.7 (53.2)	55.2 (58.6) 56.0 (58.6) 53.3 (47.2) 54.4 (54.0) 56.5 (54.0)				
NS3 (3856-4209)	PC (5)	74.7 (89)	76.1 (86.4)	76.1 (89.8)	78.0 (89.0)				
NS4 (4892-5292)	BR36 (3) HD 10 (3)	67.8 (78.5) 69.8 (74.6)	69.8 (75.1) 66.6 (69.7)	62.0 (67.5) 57.8 (59.9)					
NS4 (4936-5292)	PC (5)	61.3 (62.2)	63.0 (65.5)	52.9 (46.2)	54.3 (43.7)				
NS5b (8023-8235)	BR34 (3) BR36 (3) BR33 (3) GB358 (4a) GB549 (4b) GB809 (4c)	68.8 (76.1)	66.7 67.6 67.1 65.6 (77.0) 67.1 (77.0) 65.0 (73.5)	63.9 64.8 64.3 66.5 (70.8) 65.9 (71.7) 67.7 (69.9)	65.9 (74.4)	94.8 94.8 94.8	93.9 93.4 93.9	75.6 75.1 76.0	77.0 76.5 77.5

Shown are the nucleotide homologies (the amino-acid homology is given between brackets) for the region indicated in the left column.

Table 6. NS4 sequences of the different genotypes

prototype	ТУРЕ	SYNTHETIC PEPTIDE NS4-1 (NS4a)	SYNTHETIC PEPTIDE NS4-5 (NS4b)	SYNTHETIC PEPTIDE NS4-7 (NS4b)		
position->		1 1 6 7 9 0 0 0	1 1 7 7 2 3 0 0	1 1 7 7 3 4 0 0		
HCV-1	1a	LSG KPAHPDREV LY <u>RE</u> FDE	SQHLPYIEQ GMMLAEQFKQ K	LAEQFKQ KALGILQTAS RQA		
HCV-J	1b	LSG RPAVIPDREV LYQEFDE	as <u>h</u> lpyieq g <u>mol</u> aeqfk <u>o</u> k	<u>L</u> aeqfkq k <u>a</u> lgllqtat kqa		
HC-J6	2a	<u>VNO</u> R <u>AV</u> V <u>A</u> PDKEV LY <u>E</u> AFDE	as <u>raal</u> iee go <u>r</u> iae <u>ml</u> k <u>s</u> k	iae <u>mi</u> k <u>s</u> k <u>io</u> gilo <u>o</u> as koa		
HC-J8	2ь	L <u>ND</u> R <u>VV</u> VAPDKEĮ LY <u>B</u> APDE	as <u>k</u> a <u>al</u> iee go <u>rm</u> ae <u>mi</u> k <u>s</u> k	<u>maemlks kiq</u> gllq <u>q</u> at rqa		
BR36	3a	L <u>o</u> g kpa <u>iv</u> pdkev lyq <u>o y</u> de	SQAAPYIEQ AQYIAHQFKE K	IAHQFKE KVLGLLQRAT QQQ		
PC	5	LSG KPAIIPDRE <u>A</u> LYQ Q FDE	- a <u>as</u> lpy <u>mde_tra</u> ia <u>g</u> qfkæ k	iagofke kvlo <u>fis</u> tig <u>ok</u> a		

^{*,} residues conserved in every genotype. Underlined amino acids are type-specific, amino acids in italics are unique to type 3 and 5 sequences.

Table 7

SEQ ID NO	Primer NO (polarity)	Sequence from 5' to 3'
63	HCPr161(+)	5'-ACCGGAGGCCAGGAGAGTGATCTCCTCC-3'
64	HCPr162(-)	5'-GGGCTGCTCTATCCTCATCGACGCCATC-3'
65	HCPr163(+)	5'-GCCAGAGGCTCGGAAGGCGATCAGCGCT-3'
66	HCPr164(-)	5'-GAGCTGCTCTGTCCTCGACGCCGCA-3'
67	HCPr23(+)	5'-CTCATGGGGTACATTCCGCT-3'
68	HCPr54(-)	5'-CTATTACCAGTTCATCATCATATCCCA-3'
69	HCPr116(+)	5'-ttttAAATACATCATGRCITGYATG-3'
70	HCPr66(-)	5'-ctattaTTGTATCCCRCTGATGAARTTCCACAT-3'
7 1	HCPr118(-)	5'actagtcgactaYTGIATICCRCTIATRWARTTCCACAT-3'
72	HCPr117(+)	5'-ttttAAATACATCGCIRCITGCATGCA-3'
73	HCPr119(-)	5'-actagtcgactaRTTIGCIATIAGCCKRTTCATCCAYTG-3'
74	HCPr131(+)	5'-ggaattctagaCCITCITGGGAYGARAYITGGAARTG-3'
75	HCPr130(+)	5'-ggaattctagACIGCITAYCARGCIACIGTITGYGC-3'
76	HCPr134(+)	5'-CATATAGATGCCCACTTCCTATC-3'
77 .	HCPr3(+)	5'-GTGTGCCAGGACCATC-3'
78	HCPr4(-)	5'-GACATGCATGTCATGATGTA-3'
79	HCPr152(+)	5'-TACGCCTCTTCTATATCGGTTGGGGCCTG-3'
80	HCPr52(+)	5'-atgTTGGGTAAGGTCATCGATACCCT-3'
81	HCPr41(+)	5'-CCCGGGAGGTCTCGTAGACCGTGCA-3'
82	HCPr40(-)	5'-ctattaAAGATAGAGAAAGAGCAACCGGG-3'
124	HCPR206	5'-tggggatcccgtatgatacccgctgctttga-3'
125	HCPR207	5'-ggcggaattcctggtcatagcctccgtgaa-3'
141	HCPR109	5'-tgggatatgatgatgaactggtc-3'
142	HCPR14	5'-ccaggtacaaccgaaccaattgcc-3'

Table 8 : NS4 SEROTYPING

	Type	Pype 1 NS4		Type	Type 2 NS4		Type	Pype 3 NS4	
serum	-	5	7	1	5	7	-	s	7
type 1a									
101	60	3	9	,	-	3	;	'	6
102	_	'	7		,	7			-
103	_	3	60		- /+	3		;	٠,٠
104	3	3		7	7		6	*	. ~
105	3	3	٣	,	7	7	+	;	۱ د
106	3	_	_		_	7	‡	‡	· ;
107		3	60	,	7	7	. 7		_
108	6	3	m	٠	-/+	7	*	_	. 2
109	3	3	3	;	2	3	_		ım
110	3	3	6		‡	_			m
		-							

	Type	Type 1 NS4		Type	Type 2 NS4		Type	Type 3 NS4	
serum	1	5	7	1	5	7	1	5	7
type 1b									
Ξ	-/+	;					,	,	,
112		7			,	2	,	,	e
113	7	6		,		_	,	,	3
114	7	6		_	+	7	+	_	3
115	3	6			+	3	•		3
116	6	6	3	,	-/+	_	,	,	-
117	33	•	,	3	-/+	+	-/-		
118	_	7			-/+	2	,	+	3
119	-	7	2	'	-/+	7	+	_	7
120		e	3	- 3	- /+	;		,	,
121	3	m	3	;	7	7	7	7	3
122	m	60	-	,	_	7	7	_	_
123		33	7		-	7	,	_	_
124	60	en	3		'	7	,		7

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	Type 1	1 NS4		Type	Type 2 NS4		Type 3	3 NS4	
serum	1	2	7	1	5	4	-	ro.	7
125	е	3		1	1	3	2	-	3
126	1	7	7	-	_	_	_	_	_
127	3	7	*	,	+	_	;	· ;	7
128	3	3	6	,	'	-	. 62	;	+
129	7		3	,					. "
130		7	_	- /					
131		-	-	•					-
132		,		*		;	' +	,	
133	٣				_		. ,	_	~
134		7	7				•		•
135		3	3	_	+	7	2	_	"
136	,	3		‡	- /+	- /-	-/+		۳.
137	;	;	+		-/+	-	- /+		
138	3	3		- /-	7	7	-	+	3
type 2a									
139	3			3	3	+	_		
140	;	,		3	3	ю			,
141	7			7	-	;	7		
142					;		,	,	
143		;	- /	-	7	_	_	-/+	- /+
144	_	_	+	-	3	7	_	_	7
145	•	÷	- /+	3	_	7	7	7+	- /-
146	,	•	,	-/ +	-				
147		;		3	_	3		,	
148				;			+	,	

	Type	Type 1 NS4		Type	Type 2 NS4		Type	Type 3 NS4	
serum	1	5	7	1	5	7	1	5	7
type 2b									
149		-/+	-/+	3	3	3	7	7	‡
type 3									
150	‡	-/+	;	‡	‡	;	-	ю	3
151		,			,	,	7		7
152							3	,	
153		,						_	
154	+	_	6		;	7	7	_	6
155		7	ж		7	7	_	_	3
156	,		,						
157			,	;	‡	,	+	7	7
158	2			٠	_	7	3	7	7
159					;	*			3
160		•		٠	‡		,	7	3
161		•			_	_	‡	8	7
type 4									
162	-			-				,	
163	7	,	,	7		+	;		

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CLAIMS

- A composition comprising or consisting of at least one polynucleic acid containing 8 or more contiguous nucleotides selected from at least one of the following HCV sequences:
- an HCV type 3 genomic sequence, more particularly in any of the following regions:
 - the region spanning positions 417 to 957 of the Core/E1 region of HCV subtype
 3a,
 - the region spanning positions 4664 to 4730 of the NS3 region of HCV type 3,
 - the region spanning positions 4892 to 5292 of the NS3/4 region of HCV type
 3,
 - the region spanning positions 8023 to 8235 of the NS5 region of HCV subtype
 3a,
 - an HCV subtype 3c genomic sequence,
- an HCV subtype 2d genomic sequence,
- an HCV type 4 genomic sequence,
- the coding region of HCV subtype 5a,

with said nucleotide numbering being with respect to the numbering of HCV nucleic acids as shown in Table 1, and with said polynucleic acids containing at least one nucleotide difference with known HCV polynucleic acid sequences in the above-indicated regions, or the complement thereof.

- A composition according to claim 1, wherein said polynucleic acids correspond to a nucleotide sequence selected from any of the following HCV genomic sequences:
- an HCV genomic sequence as having a homology of at least 67%, preferably more than 69%, most preferably 71% or more to any of the sequences as represented in SEQ ID NO 13, 15, 17, 19, 21, 23, 25 or 27 in the region spanning positions 417 to 957 of the Core/E1 region;
- an HCV genomic sequence as having a homology of at least 65%, preferably more than 67%, most preferably 69% or more to any of the sequences as represented in SEQ ID NO 19, 21, 23, 25 or 27 in the region spanning positions 574 to 957 of the E1 region;
- an HCV genomic sequence, having a homology of at least 79%, more preferably at least 81%, most preferably more than 83% or more to any of the sequences as represented in

- SEQ ID NO 147 in the region spanning positions 1 to 378 of the Core region;
- an HCV genomic sequence having a homology of at least 74%, more preferably at least 76%, most preferably more than 78% or more to any of the sequences as represented in SEQ ID NO 13, 15, 17, 19, 21, 23, 25 or 27 in the region spanning positions 417 to 957 in the Core/E1 region:
- an HCV genomic sequence having a homology of at least 74%, preferably more than 76%, most preferably 78% or more to any of the sequences as represented in SEQ ID NO 13, 15, 17, 19, 21, 23, 25 or 27 in the region spanning positions 574 to 957 in the E1 region;
- an HCV genomic sequence having a homology of more than 73.5%, preferably more than 74%, most preferably 75% homology to any of the sequence as represented in SEQ ID NO 29 in the region spanning positions 4664 to 4730 of the NS3 region;
- an HCV genomic sequence having a homology of more than 70%, preferably more than 72%, most preferably more than 74% homology to any of the sequences as represented in SEQ ID NO 29, 31, 33, 35, 37 or 39 in the region spanning positions 4892 to 5292 in the NS3/NS4 region:
- an HCV genomic sequence having a homology of more than 95%, preferably 95,5%, most preferably 96% homology to any of the sequences as represented in SEQ ID NO 5,
 7, 1, 3, 9 or 11 in the region spanning positions 8023 to 8235 of the NS5 region;
- an HCV genomic sequence of the BR36 subgroup of HCV type 3a having a homology of more than 96%, preferably 96.5%, most preferably 97% homology to any of the sequences as represented in SEQ ID NO 5, 7, 1, 3, 9 or 11 in the region spanning positions 8023 to 8192 of the NS5B region;
- an HCV genomic sequence having a homology of more than 79%, more preferably more than 81%, and most preferably more than 83% to the sequence as represented in SEQ ID NO 149 in the region spanning positions 7932 to 8271 in the NS5B region.
- 3. A composition according to claim 1, wherein said polynucleic acids correspond to a nucleotide sequence selected from any of the following HCV genomic sequences:
- an HCV genomic sequence having a homology of more than 85%, preferably more than 86%, most preferably more than 87% homology to any of the sequences as represented in SEQ ID NO 41, 43, 45, 47, 49, 51, 53 or 151 in the region spanning positions 1 to 573 of the Core region;

- an HCV genomic sequence having a homology of more than 61%, preferably more than 63%, most preferably more than 65% homology to any of the sequences as represented in SEQ ID NO 41, 43, 45, 47, 49, 51, 53, 153 or 155 in the region spanning positions 574 to 957 of the El region:
- an HCV genomic sequence having a homology of more than 76.5%, preferably of more than 77%, most preferably of more than 78% homology with any of the sequences as represented in SEQ ID NO 55, 57, 197 or 199 in the region spanning positions 3856 to 4209 of the NS3 region;
- an HCV genomic sequence having a homology of more than 68%, preferably of more than 70%, most preferably of more than 72% homology with the sequence as represented in SEQ ID NO 157 in the region spanning positions 980 to 1179 of the E1/E2 region;
- an HCV genomic sequence having a homology of more than 57%, preferably more than 59%, most preferably more than 61% homology to any of the sequences as represented in SEQ ID NO 59 or 61 in the region spanning positions 4936 to 5296 of the NS4 region;
- an HCV genomic sequence having a homology of more than 93%, preferably more than 93.5%, most preferably more than 94% homology to any of the sequences as represented in SEQ ID NO 159 or 161 in the region spanning positions 7932 to 8271 of the NS5B region.
- 4. A composition according to claim 1, wherein said polynucleic acids correspond to a nucleotide sequence selected from any of the following HCV genomic sequences:
- an HCV genomic sequence having a homology of more than 66%, preferably more than 68%, most preferably more than 70% homology in the E1 region spanning positions 574 to 957 to any of the sequences as represented in SEQ ID NO 118, 120 or 122 in the region spanning positions 1 to 957 of the Core/E1 region;
- an HCV genomic sequence having a homology of more than 71%, preferably more than 72%, most preferably more than 74% homology to any of the sequences as represented in SEQ ID NO 118, 120 or 122 in the region spanning positions 379 to 957;
- an HCV genomic sequence having a homology of more than 85%, preferably more than 86%, most preferably more than 86.5% homology to any of the sequences as represented in SEQ ID NO 183, 185 or 187 in the region spanning positions 379 to 957 of the E1 region;
- an HCV genomic sequence having a homology of more than 81%, preferably more than

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83%, most preferably more than 85% homology to the sequence as represented in SEQ ID NO 189 in the region spanning positions 379 to 957 of the E1 region;

- an HCV genomic sequence having a homology of more than 85%, preferably more than 87%, most preferably more than 89% homology to any of the sequences as represented in SEQ ID NO 167 or 169 in the region spanning positions 379 to 957 of the E1 region;
- an HCV genomic sequence having a homology of more than 79%, preferably more than 81%, most preferably more than 83% homology to any of the sequences as represented in SEQ ID NO 171 or 173 in the region spanning positions 379 to 957 of the E1 region;
- an HCV genomic sequence having a homology of more than 84%, preferably more than 86%, most preferably more than 88% homology to the sequence as represented in SEQ ID NO 175 in the region spanning positions 379 to 957 of the E1 region;
- an HCV genomic sequence having a homology of more than 83%, preferably more than 85%, most preferably more than 87% homology to the sequence as represented in SEQ ID NO 177 in the region spanning positions 379 to 957 of the E1 region:
- an HCV genomic sequence having a homology of more than 76%, preferably more than 78%, most preferably more than 80% homology to the sequence as represented in SEQ ID NO 179 in the region spanning positions 379 to 957 of the E1 region;
- an HCV genomic sequence having a homology of more than 84%, preferably more than 86%, most preferably more than 88% homology to the sequence as represented in SEQ ID NO 181 in the region spanning positions 379 to 957 of the E1 region;
- an HCV genomic sequence having a homology of more than 73%, preferably more than 75%, most preferably more than 77% homology to any of the sequences as represented in SEQ ID NO 106, 108, 110, 112, 114, or 116 in the region spanning positions 7932 to 8271 of the NS5 region;
- an HCV genomic sequence having a homology of more than 88%, preferably more than 89%, most preferably more than 90% homology to any of the sequences as represented in SEQ ID NO 106, 108, 110, or 112 in the region spanning positions 7932 to 8271 of the NS5 region:
- an HCV genomic sequence having a homology of more than 88%, preferably more than 89%, most preferably more than 90% homology to any of the sequences as represented in SEQ ID NO 116 or 201 in the region spanning positions 7932 to 8271 of the NS5 region;
- an HCV genomic sequence having a homology of more than 87%, preferably more than

- 89%, most preferably more than 90% homology to the sequence as represented in SEQ ID NO 203 in the region spanning positions 7932 to 8271 of the NS5 region;
- an HCV genomic sequence having a homology of more than 85%, preferably more than 87%, most preferably more than 89% homology to the sequence as represented in SEQ ID NO 114 in the region spanning positions 7932 to 8271 of the NS5 region;
- an HCV genomic sequence having a homology of more than 86%, preferably more than 87%, most preferably more than 88% homology to the sequence as represented in SEQ ID NO 207 in the region spanning positions 7932 to 8271 of the NS5 region;
- an HCV genomic sequence having a homology of more than 84%, preferably more than 86%, most preferably more than 88% homology to the sequence as represented in SEQ ID NO 209 in the region spanning positions 7932 to 8271 of the NS5 region;
- an HCV genomic sequence having a homology of more than 81%, preferably more than 83%, most preferably more than 85% homology to the sequence as represented in SEQ ID NO 211 in the region spanning positions 7932 to 8271 of the NS5 region.
- A composition according to claim 1, wherein said polynucleic acids correspond to a nucleotide sequence selected from any of the following HCV genomic sequences:
- an HCV genomic sequence having a homology of more than 78%, preferably more than 80%, most preferably more than 82% homology to the sequence as represented in SEQ ID NO 143 in the region spanning positions 379 to 957 of the Core/E1 region;
- an HCV genomic sequence having a homology of more than 74%, preferably more than 76%, most preferably more than 78% homology to the sequence as represented in SEQ ID NO 143 in the region spanning positions 574 to 957;
- an HCV genomic sequence having a homology of more than 87%, preferably more than 89%, most preferably more than 91% homology to the sequence as represented in SEQ ID NO 145 in the region spanning positions 7932 to 8271 of the NS5B region.
- 6. A composition according to any of claims 1 to 5, wherein said polynucleic acid is liable to act as a primer for amplifying the nucleic acid of a certain isolate belonging to the genotype from which the primer is derived.
- A composition according to any of claims 1 to 5, wherein said polynucleic acid is able to act as a hybridization probe for specific detection and/or classification into types of a

nucleic acid containing said nucleotide sequence, with said oligonucleotide being possibly labelled or attached to a solid substrate.

- 8. Use of a composition according to any of claims 1 to 7 for in vitro detecting the presence of one or more HCV genotypes, more particularly for detecting the presence of a nucleic acid of any of the HCV genotypes having a nucleotide sequence as defined in any of claims 1 to 5, present in a biological sample liable to contain them, comprising at least the following steps:
 - (i) possibly extracting sample nucleic acid,
 - (ii) possibly amplifying the nucleic acid with at least one of the primers according to claim 6 or any other HCV type 2, HCV type 3, HCV type 4, HCV type 5 or universal HCV primer,
 - (iii) hybridizing the nucleic acids of the biological sample, possibly under denatured conditions, and with said nucleic acids being possibly labelled during or after amplification, at appropriate conditions with one or more probes according to claim 7, with said probes being preferably attached to a solid substrate,
 - (iv) washing at appropriate conditions,
 - (v) detecting the hybrids formed,
 - (vi) inferring the presence of one or more HCV genotypes present from the observed hybridization pattern.
- 9. A composition consisting of or comprising at least one peptide or polypeptide containing in its sequence a contiguous sequence of at least 5 amino acids of an HCV polyprotein encoded by any of the polynucleic acids according to any of claims 1 to 5.
- 10. A composition according to claim 9, wherein said contiguous sequence contains in its sequence at least one of the following amino acid residues:
- L7, Q43, M44, S60, R67, Q70, T71, A79, A87, N106, K115, A127, A190, S130, V134, G142, I144, E152, A157, V158, P165, S177 or Y177, I178, V180 or E180 or F182, R184, I186, H187, T189, A190, S191 or G191, Q192 or L192 or I192 or V192 or E192, N193 or H193 or P193, W194 or Y194, H195, A197 or I197 or V197 or T197, V202, I203 or L203, Q208, A210, V212, F214, T216, R217 or D217 or E217 or V217, H218 or N218, H219 or V219 or L219, L227 or I227, M231 or E231 or Q231, T232 or D232 or A232 or K232, Q235

or I235, A237 or T237, I242, I246, S247, S248, V249, S250 or Y250, I251 or V251 or M251 or F251, D252, T254 or V254, L255 or V255, E256 or A256, M258 or F258 or V258, A260 or Q260 or S260, A261, T264 or Y264, M265, I266 or A266, A267, G268 or T268, F271 or M271 or V271, I277, M280 or H280, I284 or A284 or L84, V274, V291, N292 or S292, R293 or I293 or Y293, Q294 or R294, L297 or I297 or Q297, A299 or K299 or Q299, N303 or T303, T308 or L308, T310 or F310 or A310 or D310 or V310, L313, G317 or O317. L333, S351, A358, A359, A363, S364, A366, T369, L373, F376, O386, I387, S392, I399, F402, I403, R405, D454, A461, A463, T464, K484, Q500, E501, S521, K522, H524, N528, S531, S532, V534, F536, F537, M539, I546, C1282, A1283, H1310, V1312, Q1321, P1368, V1372, V1373, K1405, Q1406, S1409, A1424, A1429, C1435, S1436, S1456, H1496, A1504, D1510, D1529, I1543, N1567, D1556, N1567, M1572, O1579, L1581, S1583, F1585, V1595, E1606 or T1606, M1611, V1612 or L1612, P1630, C1636, P1651, T1656 or I1656, L1663, V1667, V1677, A1681, H1685, E1687, G1689, V1695, A1700, O1704, Y1705, A1713, A1714 or S1714, M1718, D1719, A1721 or T1721, R1722, A1723 or V1723, H1726 or G1726, E1730, V1732, F1735, I1736, S1737, R1738, T1739, G1740, Q1741, K1742, Q1743, A1744, T1745, L1746, E1747 or K1747, I1749, A1750, T1751 or A1751, V1753, N1755, K1756, A1757, P1758, A1759, H1762, T1763, Y1764, P2645, A2647, K2650, K2653 or L2653, S2664, N2673, F2680, K2681, L2686, H2692, Q2695 or L2695 or I2695, V2712, F2715, V2719 or O2719, T2722, T2724, S2725, R2726, G2729, Y2735, H2739, I2748, G2746 or 12746, I2748, P2752 or K2752, P2754 or T2754, T2757 or P2757.

with said notation being composed of a letter representing the amino acid residue by its oneletter code, and a number representing the amino acid numbering according to Kato et al.,

- 11. A composition according to any of claims 9 or 10, wherein said contiguous sequence is selected from any of the following HCV amino acid sequences:
- a sequence having a homology of more than 72%, preferably more than 74%, and most preferably more than 77% homology to any of the amino acid sequences as represented in SEQ ID NO 14, 16, 18, 20, 22, 24, 26 or 28 in the region spanning positions 140 to 319 in the Core/E1 region:
- a sequence having a homology of more than 70%, preferably more than 72%, and most preferably more than 75% homology to any of the amino acid sequences as represented in SEO ID NO 14, 16, 18, 20, 22, 24, 26 or 28 in the E1 region spanning positions 192 to

319:

- a sequence having a homology of more than 86%, preferably more than 88%, and most preferably more than 90% homology to the amino acid sequences as represented in SEQ ID NO 148 in the region spanning positions 1 to 110 in the Core region:
- a sequence having a homology of more than 76%, preferably more than 78%, most preferably more than 80% to any of the amino acid sequences as represented in SEQ ID NO 30, 32, 34, 36, 38 or 40 in the region spanning positions 1646 to 1764 in the NS3/NS4 region;
- a sequence having a homology of more than 81.5%, preferably more than 83%, and most preferably more than 86% homology to any of the amino acid sequences as represented in SEQ ID NO 14, 16, 18, 20, 22, 24, 26 or 28 in the E1 region spanning positions 192 to 319:
- a sequence having a homology of more than 86%, preferably more than 88%, most preferably more than 90% to the amino acid sequence as represented in SEQ ID NO 150 in the region spanning positions 2645 to 2757 in the NSSB region;
- 12. A composition according to any of claims 9 or 10, wherein said contiguous sequence is selected from any of the following HCV amino acid sequences:
- a sequence having a homology of more than 80%, preferably more than 82%, most preferably more than 84% homology to any of the amino acid sequences as represented in SEQ ID NO 118, 120, and 122 in the region spanning positions 127 to 319,
- a sequence having a homology of more than 73%, preferably more than 75%, most preferably more than 78% homology in the E1 region spanning positions 192 to 319 to any of the amino acid sequences as represented in SEQ ID NO 118, 120, and 122, in the region spanning positions 127 to 319.
- a sequence having more than 85%, preferably more than 86%, most preferably more than 87% homology to any of the amino acid sequences as represented in SEQ ID NO 118, 120 or 122, in the region spanning positions 192 to 319.
- 13. A composition according to any of claims 9 or 10, wherein said contiguous sequence is selected from any of the following HCV amino acid sequences:
- a sequence having more than 93%, preferably more than 94%, most preferably more than
 95% homology in the region spanning Core positions 1 to 191 to any of the amino acid

- sequences as represented in SEQ ID NO 42, 44, 46, 48, 50, 52, 54, or 152;
- a sequence having more than 73%, preferably more than 74%, most preferably more than 76% homology in the region spanning E1 positions 192 to 319 to any of the amino acid sequences as represented in SEQ ID NO 42, 44, 46, 48, 50, 52, 54, 154 or 156;
- a sequence spanning positions 1286 to 1403 of the NS3 region, with said sequence being characterized as having more than 90%, preferably more than 91%, most preferably more than 92% homology to any of the amino acid sequences represented in SEQ ID NO 56 to 58:
- a sequence spanning positions 1646 to 1764 of the NS3/4 region, with said sequence being characterized as having more than 66%, more particularly 68%, most particularly 70% or more homology to any of the amino acid sequences as represented in SEQ ID NO 60 or 62.
- 14. A composition according to any of claims 9 to 10, wherein said contiguous sequence is selected from any of the following HCV amino acid sequences:
- a sequence having a more than 83%, preferably more than 85%, most preferably more than 87% homology in the region spanning Core positions 1 to 319 to the amino acid sequence as represented in SEQ ID NO 144;
- a sequence having a more than 79%, preferably more than 81%, most preferably more than 84% homology in the region spanning E1 positions 192 to 319 to the amino acid sequence as represented in SEO ID NO 144;
- a sequence having more than 95%, more particularly 96%, most particularly 97% or more homology to the amino acid sequence as represented in SEQ ID NO 146, in the region spanning positions 2645 to 2757 of the NS5B region.
- 15. A composition according to any of claims 9 to 14, wherein said sequence is selected from the following peptides:

QPTGRSWGQ (SEQ ID NO 93)

RSEGRTSWAQ (SEQ ID NO 220)

RTEGRTSWAQ (SEQ ID NO 221)

SRROPIPRARRTEGRSWAQ (SEQ ID NO 268)

LEWRNTSGLYVL (SEQ ID NO 83)

VNYRNASGIYHI (SEO ID NO 126)

QHYRNISGIYHV (SEQ ID NO 127) EHYRNASGIYHI (SEQ ID NO 128) IHYRNASGIYHI (SEQ ID NO 224) VPYRNASGIYHV (SEQ ID NO 84) VNYRNASGIYHI (SEQ ID NO 225) VNYRNASGVYHI (SEQ ID NO 226) VNYHNTSGIYHL (SEO ID NO 227) OHYRNASGIYHV (SEQ ID NO 228) QHYRNVSGIYHV (SEQ ID NO 229) IHYRNASDGYYI (SEQ ID NO 230) LQVKNTSSSYMV (SEQ ID NO 231) VYEADDVILHT (SEQ ID NO 85) VYETEHHILHL (SEQ ID NO 129) VYEADHHIMHL (SEQ ID NO 130) VYETDHHILHL (SEO ID NO 131) VYEADNLILHA (SEQ ID NO 86) VWQLRAIVLHV (SEQ ID NO 232) VYEADYHILHL (SEQ ID NO 233) VYETDNHILHL (SEQ ID NO 234) VYETENHILHL (SEQ ID NO 235) VFETVHHILHL (SEO ID NO 236) VFETEHHILHL (SEQ ID NO 237) VFETDHHIMHL (SEQ ID NO 238) VYETENHILHL (SEQ ID NO 239) VYEADALILHA (SEQ ID NO 240) VQDGNTSTCWTPV (SEQ ID NO 87) VODGNTSACWTPV (SEQ ID NO 241) VRVGNQSRCWVAL (SEQ ID NO 132) VRTGNTSRCWVPL (SEQ ID NO 133) VRAGNVSRCWTPV (SEO ID NO 134) EEKGNISRCWIPV (SEQ ID NO 242) VKTGNQSRCWVAL (SEQ ID NO 243)

VRTGNQSRCWVAL (SEQ ID NO 244)

VKTGNOSRCWIAL (SEQ ID NO 245)

VKTGNVSRCWIPL (SEQ ID NO 247)

VKTGNVSRCWISL (SEQ ID NO 248)

VRKDNVSRCWVOI (SEO ID NO 249)

VRYVGATTAS (SEQ ID NO 89)

APYIGAPLES (SEQ ID NO 135)

APYVGAPLES (SEQ ID NO 136)

AVSMDAPLES (SEQ ID NO 137)

APSLGAVTAP (SEQ ID NO 90)

APSFGAVTAP (SEQ ID NO 250)

VSQPGALTKG (SEQ ID NO 251)

VKYVGATTAS (SEQ ID NO 252)

APYIGAPVES (SEQ ID NO 253)

AQHLNAPLES (SEQ ID NO 254)

SPYVGAPLEP (SEQ ID NO 255) SPYAGAPLEP (SEQ ID NO 256)

APYLGAPLEP (SEQ ID NO 257)

APYLGAPLES (SEQ ID NO 258)

APYVGAPLES (SEQ ID NO 259)

VPYLGAPLTS (SEQ ID NO 260)

APHLRAPLSS (SEQ ID NO 261)

APYLGAPLTS (SEQ ID NO 262)

RPRRHQTVQT (SEQ ID NO 91)

QPRRHWTTQD (SEQ ID NO 138)

RPRRHWTTQD (SEQ ID NO 139)

RPRQHATVQN (SEQ ID NO 92)

RPRQHATVQD (SEQ ID NO 263)

SPQHHKFVQD (SEQ ID NO 264)

RPRRLWTTQE (SEQ ID NO 265)

PPRIHETTQD (SEQ ID NO 266)

TISYANGSGPSDDK (SEQ ID NO 267)

^{16.} Recombinant vector, particularly for cloning and/or expression, with said recombinant

vector comprising a vector sequence, an appropriate prokaryotic, eukaryotic or viral promoter sequence followed by the nucleotide sequences as defined in claims 1 to 5, with said recombinant vector allowing the expression of any one of the HCV type 2 and/or HCV type 3 and/or type 4 and/or type 5 derived polypeptides according to any of claims 9 to 15 in a prokaryotic, or eukaryotic host, or in living mammals when injected as naked DNA, and more particularly a recombinant vector allowing the expression of any of the following HCV type 2. HCV type 3, type 4 or type 5 polypeptides spanning the following amino acid positions:

- a polypeptide starting at position 1 and ending at any position in the region between positions 70 and 326, more particularly a polypeptide spanning positions 1 to 70, 1 to 85, positions 1 to 120, positions 1 to 150, positions 1 to 191, positions 1 to 200, for expression of the Core protein, and positions 1 to 263, positions 1 to 326, for expression of the Core and E1 protein;
- a polypeptide starting at any position in the region between positions 117 and 192, and ending at any position in the region between positions 263 and 326, more particularly from positions 119 to 326, for expression of E1, or forms that have the putative membrane anchor deleted (positions 264 to 293 plus or minus 8 amino acids);
- a polypeptide starting at any position in the region between positions 1556 and 1688, and ending at any position in the region between positions 1739 and 1764, for expression of the NS4 regions, more particularly a polypeptide starting at position 1658 and ending at position 1711 for expression of the NS4a antigen, and more particularly, a polypeptide starting at position 1712 and ending between positions 1743 and 1972, for example 1712-1743, 1712-1764, 1712-1782, 1712-1972, 1712 to 1782 and 1902 to 1972 for expression of the NS4b protein or parts thereof.
- 17. A composition according to any of claims 9 to 15, wherein said polypeptide is a recombinant polypeptide expressed by means of an expression vector as defined in claim 16.
- 18. A composition according to any of claims 9 to 15 or 16, for use in a method for immunizing a mammal, preferably humans, against HCV comprising administratering a sufficient amount of the composition possibly accompanied by pharmaceutically acceptable adjuvants, to produce an immune response, more particularly a vaccine composition including HCV type 3 polypeptides derived from the E1, Core, or NS4 region and/or type 4 and/or type 5 and/or type 2 polypeptides.

- 19. Antibody raised upon immunization with a composition according to any of claims 9 to 15, 17 or 18, by means of a process according to claim 18, with said antibody being reactive with any of the polypeptides as defined in any of claims 9 to 15, 17 or 18.
- 20. Process for detecting in vitro HCV present in biological sample liable to contain it, comprising at least the following steps:
 - (i) contacting the biological sample to be analyzed for the presence of HCV antibodies with any of the compositions according to claims 9 to 15, 17 or 18, preferentially in an immobilized form under appropriate conditions which allow the formation of an immune complex, wherein said polypeptide is preferentially in the form of a biotinylated polypeptide and is covalently bound to a solid substrate by means of streptavidin or avidin complexes,
 - (ii) removing unbound components,
 - (iii) incubating the immunecomplexes formed with heterologous antibodies, which specifically bind to the antibodies present in the sample to be analyzed, with said heterologous antibodies having conjugated to a detectable label under appropriate conditions,
 - (iv) detecting the presence of said immunecomplexes visually or by means of densitometry and inferring the HCV serotype(s) present from the observed hybridization pattern.
- 21. Use of a composition according to any of claims 9 to 15, 17 or 18, for incorporation into a serotyping assay for detecting one or more serological types of HCV present in a biological sample liable to contain it, more particularly for detecting E1 and NS4 antigens or antibodies of the different types to be detected combined in one assay format, comprising at least the following steps:
 - (i) contacting the biological sample to be analyzed for the presence of HCV antibodies or antigens of one or more serological types, with at least one of the compositions according to claims 9 to 15, 17 or 18 in an immobilized form under appropriate conditions which allow the formation of an immunecomplex, (wherein said polypeptide is preferentially in the form of a biotinylated polypeptide and is covalently bound to a solid substrate by means of streptavidin or avidin complexes),

- (ii) removing unbound components,
- (iii) incubating the immunecomplexes formed with heterologous antibodies, which specifically bind to the antibodies present in the sample to be analyzed, with said heterologous antibodies having conjugated to a detectable label under appropriate conditions,
- (iv) detecting the presence of said immunecomplexes visually or by means of densitometry and inferring the HCV serological types present from the observed binding pattern.
- 22. A kit for determining the presence of HCV genotypes as defined in any of claims 1 to 5 present in a biological sample liable to contain them, comprising:
 - possibly at least one primer composition containing any primer selected from those defined in claim 6 or any other HCV type 2 and/or HCV type 3 and/or HCV type 4 and/or HCV type 5, or universal HCV primers,
 - at least one probe composition according to claim 7, preferably in combination with other polypeptides or peptides from HCV type 1, type 2 or other types of HCV, with said probes being preferentially immobilized on a solid substrate, and more preferentially on one and the same membrane strip,
 - a buffer or components necessary for producing the buffer enabling hybridization reaction between these probes and the possibly amplified products to be carried out,
 - a means for detecting the hybrids resulting from the preceding hybriziation,
 - possibly also including an automated scanning and interpretation device for infering the HCV genotype(s) present in the sample from the observed hybridization pattern.
- 23. A kit for determining the presence of HCV antibodies according to any of claims 9 to 15, 17 or 18 present in a biological sample liable to contain them, comprising:
 - at least one polypeptide composition according to any of claims 9 to 15, 17 or 18, with said polypeptides being preferentially immobilized on a solid substrate, and more preferentially on one and the same membrane strip,
 - a buffer or components necessary for producing the buffer enabling binding reaction between these polypeptides and the antibodies against HCV present in the biological sample.
 - a means for detecting the immune complexes formed in the preceding binding

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reaction,

 possibly also including an automated scanning and interpretation device for infering the HCV genotype present in the sample from the observed binding pattern.

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SUBSTITUTE SHEET (RULE 26)

SECUENCE LISTING

- (1) GENERAL INFORMATION:
 - (i) APPLICANT:
 - (A) NAME: Innogenetics sa.
 - (B) STREET: Industriepark Zwijnaarde 7, box 4
 - (C) CITY: Ghent
 - (E) COUNTRY: Belgium
 - (F) POSTAL CODE (ZIP): B-9052
 - (G) TELEPHONE: 00 32 9 241 07 11
 - (H) TELEFAX: 00 32 9 241 07 99
 - (ii) TITLE OF INVENTION: New sequences of hepatitis C virus genotypes for diagnosis, prophylaxis and therapy.
 - (iii) NUMBER OF SEQUENCES: 270
 - (iv) COMPUTER READABLE FORM:
 - (A) MEDIUM TYPE: Floppy disk
 - (B) COMPUTER: IBM PC compatible
 - (C) OPERATING SYSTEM: PC-DOS/MS-DOS
 - (D) SOFTWARE: PatentIn Release #1.0, Version #1.25 (EPO)
- (2) INFORMATION FOR SEQ ID NO: 1:
 - (i) SEQUENCE CHARACTERISTICS:
 - (A) LENGTH: 213 base pairs
 - (B) TYPE: nucleic acid
 - (C) STRANDEDNESS: single
 (D) TOPOLOGY: linear
 - (ii) MOLECULE TYPE: cDNA
 - (iii) HYPOTHETICAL: NO
 - (iii) ANTI-SENSE: NO
 - (vii) IMMEDIATE SOURCE:
 - (B) CLONE: BR34-4-20
 - (ix) FEATURE:
 - (A) NAME/KEY: CDS
 - (B) LOCATION: 1..213
 - (xi) SEQUENCE DESCRIPTION: SEQ ID NO: 1:
- CTC ACG GAA CGG CTT TAC TGC GGG GGC CCT ATG TTC AAC AGC AAG GGG Leu Thr Glu Arg Leu Tyr Cys Gly Gly Pro Met Phe Asn Ser Lys Gly
- GCC CAG TGT GGT TAT CGC CGC TGC CGT GCC AGT GGA GTT CTG CCT ACC
 Ala Gln Cys Gly Tyr Arg Arg Cys Arg Ala Ser Gly Val Leu Pro Thr

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AGC TTC GGC AAC ACA ATC ACT TGC TAC ATC AAG GCC ACA GCG GCT GCA Ser Phe Gly Asn Thr Ile Thr Cys Tyr Ile Lys Ala Thr Ala Ala Ala 35 40

Arg Ala Ala Gly Leu Arg Asn Pro Asp Phe Leu Val Cys Gly Asp Asp

AGG GCC GCA GGC CTC CGG AAC CCG GAC TTT CTT GTC TGC GGA GAT GAT 192

CTG GTC GTG GTG GCT GAG AGT Leu Val Val Ala Glu Ser

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- (2) INFORMATION FOR SEO ID NO: 2:
 - (i) SEQUENCE CHARACTERISTICS: (A) LENGTH: 71 amino acids
 - (B) TYPE: amino acid
 - (D) TOPOLOGY: linear
 - (ii) MOLECULE TYPE: protein
 - (xi) SEQUENCE DESCRIPTION: SEQ ID NO: 2:

Leu Thr Glu Arg Leu Tyr Cys Gly Gly Pro Met Phe Asn Ser Lys Gly 1

Ala Gln Cys Gly Tyr Arg Arg Cys Arg Ala Ser Gly Val Leu Pro Thr

Ser Phe Gly Asn Thr Ile Thr Cys Tyr Ile Lys Ala Thr Ala Ala Ala

Arg Ala Ala Gly Leu Arg Asn Pro Asp Phe Leu Val Cys Gly Asp Asp

Leu Val Val Val Ala Glu Ser

- (2) INFORMATION FOR SEQ ID NO: 3:
 - (i) SEQUENCE CHARACTERISTICS:
 - (A) LENGTH: 213 base pairs
 - (B) TYPE: nucleic acid
 - (C) STRANDEDNESS: single
 - (D) TOPOLOGY: linear
 - (ii) MOLECULE TYPE: cDNA
 - (vii) IMMEDIATE SOURCE:
 - __ (B) CLONE: BR36-23-18
 - (ix) FEATURE:
 - (A) NAME/KEY: CDS
 - (B) LOCATION: 1..213

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(xi)	SEQUENCE	DESCRIPTION:	SEO	TD	NO .	2.

	ACG Thr															48
	CAG Gln															96
	TTC Phe															144
AGG Arg	GCC Ala 50	GCA Ala	GGC Gly	CTC Leu	CGG Arg	AAC Asn 55	CCG Pro	GAC Asp	TTT Phe	CTT Leu	GTC Val 60	TGC Cys	GGA Gly	GAT Asp	GAT Asp	192
	GTC Val															213

- (2) INFORMATION FOR SEQ ID NO: 4:
 - (i) SEQUENCE CHARACTERISTICS:

70

- (A) LENGTH: 71 amino acids
- (B) TYPE: amino acid (D) TOPOLOGY: linear
- (ii) MOLECULE TYPE: protein
- (xi) SEQUENCE DESCRIPTION: SEQ ID NO: 4:

Leu Thr Glu Arg Leu Tyr Cys Gly Gly Pro Met Phe Asn Ser Lys Gly

1 10 15

Ala Gln Cys Gly Tyr Arg Arg Cys Arg Ala Ser Gly Val Leu Pro Thr 20 25 30

Ser Phe Gly Asn Thr Ile Thr Cys Tyr Ile Lys Ala Thr Ala Ala Ala 35 40 45

Arg Ala Ala Gly Leu Arg Asn Pro Asp Phe Leu Val Cys Gly Asp Asp
50 55 60

Leu Val Val Val Ala Glu Ser

- (2) INFORMATION FOR SEQ ID NO: 5:
 - (i) SEQUENCE CHARACTERISTICS:
 - (A) LENGTH: 213 base pairs
 - (B) TYPE: nucleic acid
 - (C) STRANDEDNESS: single
 - (D) TOPOLOGY: linear

48

96

98	
(ii) MOLECULE TYPE: cDNA	
(iii) HYPOTHETICAL: NO	
(iii) ANTI-SENSE: NO	
(vii) IMMEDIATE SOURCE: (B) CLONE: BR36-23-18	
(ix) FEATURE: (A) NAME/KEY: CDS (B) LOCATION: 1213	
(xi) SEQUENCE DESCRIPTION: SEQ ID NO: 5:	
CTC ACG GAG CGG CTT TAC TGC GGG GGC CCT ATG TTT AAC AGC AAG GGG Leu Thr Glu Arg Leu Tyr Cys Gly Gly Pro Met Phe Asn Ser Lys Gly 1 5 10 15	48
GCC CAG TGT GGT TAT CGC CGT TGC CGT GCC AGT GGA GTT CTG CCT ACC Ala Gln Cys Gly Tyr Arg Arg Cys Arg Ala Ser Gly Val Leu Pro Thr 20 25 30	96
AGC TTC GGC AAC ACA ATC ACT TGT TAC ATC AAA GGC ACA GGG GGC GGA Ser Phe Gly Asn Thr Ile Thr Cys Tyr Ile Lys Ala Thr Ala Ala Ala 35 45	144
AAA GCC GCA GGC CTC CGG AGC CCG GAC TTT CTT GTC TGC GGA GAT GAT Lys Ala Ala Gly Leu Arg Ser Pro Asp Phe Leu Val Cys Gly Asp Asp 50 55 60	192
CTG GTC GTG GCT GAG AGT Leu Val Val Ala Glu Ser 65 70	213
(2) INFORMATION FOR SEQ ID NO: 6:	
(i) SEQUENCE CHARACTERISTICS: (A) LENGTH: 71 amino acids (B) TYPE: amino acid (D) TOPOLOGY: linear	
(ii) MOLECULE TYPE: protein	
(xi) SEQUENCE DESCRIPTION: SEQ ID No: 6:	
Leu Thr Glu Arg Leu Tyr Cys Gly Gly Pro Met Phe Asn Ser Lys Gly $1 \ 5 \ 10 \ 15$	
Ala Gln Cys Gly Tyr Arg Arg Cys Arg Ala Ser Gly Val Leu Pro Thr 20 30	
Ser Phe Gly Asn Thr Ile Thr Cys Tyr Ile Lys Ala Thr Ala Ala Ala 35	

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Lys Ala Ala Gly Leu Arg Ser Pro Asp Phe Leu Val Cys Gly Asp Asp

Leu Val Val Val Ala Glu Ser

- (2) INFORMATION FOR SEQ ID NO: 7:
 - (i) SEQUENCE CHARACTERISTICS:
 - (A) LENGTH: 213 base pairs
 - (B) TYPE: nucleic acid
 - (C) STRANDEDNESS: single (D) TOPOLOGY: linear

 - (ii) MOLECULE TYPE: cDNA
 - (iii) HYPOTHETICAL: NO
 - (iii) ANTI-SENSE: NO
 - (vii) IMMEDIATE SOURCE:
 - (B) CLONE: BR36-23-20
 - (ix) FEATURE:
 - (A) NAME/KEY: CDS
 - (B) LOCATION: 1..213
 - (xi) SEQUENCE DESCRIPTION: SEQ ID NO: 7:

CTC ACG GAG CGG CTT TAC TGC GGG GGC CCT ATG TTT AAC AGC AAA GGG 48 Leu Thr Glu Arg Leu Tyr Cys Gly Gly Pro Met Phe Asn Ser Lys Gly 1

GCC CAG TGT GGT TAT CGC CGT TGC CGT GCC AGT GGA GTT CTG CCT ACC 96 Ala Gln Cys Gly Tyr Arg Arg Cys Arg Ala Ser Gly Val Leu Pro Thr 20

AGC TTC GGC AAC ACA ATC ACT TGT TAC ATC AAA GCC ACA GCG GCC GCA 144 Ser Phe Gly Asn Thr Ile Thr Cys Tyr Ile Lys Ala Thr Ala Ala Ala 40

AAA GCC GCA GGC CTC CGG AGC CCG GAC TTT CTT GTC TGC GGA GAT GAT 192 Lys Ala Ala Gly Leu Arg Ser Pro Asp Phe Leu Val Cys Gly Asp Asp 55

CTG GTC GTG GTG GCT GAG AGT 213 Leu Val Val Val Ala Glu Ser

- (2) INFORMATION FOR SEO ID NO: 8:
 - (i) SEQUENCE CHARACTERISTICS:
 - (A) LENGTH: 71 amino acids (B) TYPE: amino acid

 - (D) TOPOLOGY: linear

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ı	11:11	MOLECULE	TYPE -	protein

(ned)	CHOTTENCE	DECCETOTION.	CEO	TD	NO.	ο.	

Leu Thr Glu Arg Leu Tyr Cys Gly Gly Pro Met Phe Asn Ser Lys Gly
1 5 10 15

Ala Gln Cys Gly Tyr Arg Arg Cys Arg Ala Ser Gly Val Leu Pro Thr 20 25 30

Ser Phe Gly Asn Thr Ile Thr Cys Tyr Ile Lys Ala Thr Ala Ala Ala 35 40 45

Lys Ala Ala Gly Leu Arg Ser Pro Asp Phe Leu Val Cys Gly Asp Asp 50 55 60

Leu Val Val Val Ala Glu Ser

(2) INFORMATION FOR SEQ ID NO: 9:

- (i) SEQUENCE CHARACTERISTICS:
 - (A) LENGTH: 213 base pairs
 - (B) TYPE: nucleic acid
 - (C) STRANDEDNESS: single
 (D) TOPOLOGY: linear
- (ii) MOLECULE TYPE: cDNA
- (iii) HYPOTHETICAL: NO
 (iii) ANTI-SENSE: NO
- (vii) IMMEDIATE SOURCE:
 (B) CLONE: BR33-2-17
- (ix) FEATURE:
 - (A) NAME/KEY: CDS
 - (B) LOCATION: 1..213
- (xi) SEQUENCE DESCRIPTION: SEQ ID NO: 9:

CTC ACG GAG CGG CTT TAC TGC GGG GGC CCT ATG TTC AAC AGC AAG GGG
Leu Thr Glu Arg Leu Tyr Cys Gly Gly Pro Met Phe Asn Ser Lys Gly

GCC CAG TGT GGT TAT CGC CGT TGT CGT GCC AGT GGA GTT CTG CCT ACC Ala Gln Cys Gly Tyr Arg Arg Cys Arg Ala Ser Gly Val Leu Pro Thr

AGT TTC GGC AAC ACA ATC ACT TGT TAC ATC AAG GCC ACA GCG GCT GCA

Ser Phe Gly Asn Thr Ile Thr Cys Tyr Ile Lys Ala Thr Ala Ala Ala

40

45

45

AAA GCC GCA GGC CTC CGG AAC CCG GAC TTT CTT GTT TGC GGA GAT GAT 192

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101 Lys Ala Ala Gly Leu Arg Asn Pro Asp Phe Leu Val Cys Gly Asp Asp

TTG GTC GTG GTG GCT GAG AGT Leu Val Val Val Ala Glu Ser

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- (2) INFORMATION FOR SEQ ID NO: 10:
 - (i) SEQUENCE CHARACTERISTICS:
 - (A) LENGTH: 71 amino acids
 - (B) TYPE: amino acid
 - (D) TOPOLOGY: linear
 - (ii) MOLECULE TYPE: protein
 - (xi) SEQUENCE DESCRIPTION: SEQ ID NO: 10:

Leu Thr Glu Arg Leu Tyr Cys Gly Gly Pro Met Phe Asn Ser Lys Gly

Ala Gln Cys Gly Tyr Arg Arg Cys Arg Ala Ser Gly Val Leu Pro Thr 20 30

Ser Phe Gly Asn Thr Ile Thr Cys Tyr Ile Lys Ala Thr Ala Ala Ala

Lys Ala Ala Gly Leu Arg Asn Pro Asp Phe Leu Val Cys Gly Asp Asp

Leu Val Val Val Ala Glu Ser 65

- (2) INFORMATION FOR SEQ ID NO: 11:
 - (i) SEQUENCE CHARACTERISTICS:
 - (A) LENGTH: 213 base pairs
 - (B) TYPE: nucleic acid
 - (C) STRANDEDNESS: single (D) TOPOLOGY: linear
 - (ii) MOLECULE TYPE: cDNA

 - (iii) HYPOTHETICAL: NO
 - (iii) ANTI-SENSE: NO
 - (vii) IMMEDIATE SOURCE:
 - (B) CLONE: BR33-2-21
 - (ix) FEATURE:
 - (A) NAME/KEY: CDS (B) LOCATION: 1..213
 - (xi) SEQUENCE DESCRIPTION: SEQ ID NO: 11:

- (2) INFORMATION FOR SEO ID NO: 12:
 - (i) SEQUENCE CHARACTERISTICS:
 - (A) LENGTH: 71 amino acids
 - (B) TYPE: amino acid (D) TOPOLOGY: linear
 - (ii) MOLECULE TYPE: protein
 - (xi) SEQUENCE DESCRIPTION: SEQ ID NO: 12:

Leu Thr Glu Arg Leu Tyr Cys Gly Gly Pro Met Phe Asn Ser Lys Gly
1 5 10 15

Ala Gln Cys Gly Tyr Arg Arg Cys Arg Ala Ser Gly Val Leu Pro Thr

Ser Phe Gly Asn Thr Ile Thr Cys Tyr Ile Lys Ala Thr Ala Ala Ala 35 40 45

Lys Ala Ala Gly Leu Arg Asn Pro Asp Phe Leu Val Cys Gly Asp Asp
50 55 60

Leu Val Val Val Ala Glu Ser

- (2) INFORMATION FOR SEQ ID NO: 13:
 - (i) SEQUENCE CHARACTERISTICS:
 - (A) LENGTH: 541 base pairs
 - (B) TYPE: nucleic acid
 - (C) STRANDEDNESS: single
 - (D) TOPOLOGY: linear
 - (ii) MOLECULE TYPE: cDNA
 - (iii) HYPOTHETICAL: NO

(iii)	ANTI-SENSE:	NO
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(vii) IMMEDIATE SOURCE: (B) CLONE: HD10-2-5

(ix) FEATURE:

(A) NAME/KEY: CDS (B) LOCATION: 2..541

(xi) SEQUENCE DESCRIPTION: SEQ ID NO: 13:	
C GTC GGC GCT CCT GTA GGA GGC GTC GCA AGA GCC CTT GGG CAT GGC Val Gly Ala Pro Val Gly Gly Val Ala Arg Ala Leu Ala His Gly 1 5 10	46
GTG AGG GCC CTT GAA GAC GGG ATA AAT TTC GCA ACA GGG AAT TTG CCC Val Arg Ala Leu Glu Asp Gly 1le Asn Phe Ala Thr Gly Asn Leu Pro $20 \hspace{1cm} 25 \hspace{1cm} 30$	94
GGT TGC TCC TTT TCT ATC TTC CTT CTT GCT CTG TTC TCT TGC TTA ATC Gly Cys Ser Phe Ser Ile Phe Leu Leu Ala Leu Phe Ser Cys Leu Ile $35 \hspace{1cm} 40 \hspace{1cm} 45$	142
CAT CCA GCA GCT AGT CTA GAG TGG CGG AAC ACG TCT GGC CTC TAT GTC His Pro Ala Ala Ser Leu Glu Trp Arg Asn Thr Ser Gly Leu Tyr Val $$50\ $	190
CTT ACC AAC GAC TGT TCC AAT AGC AGT ATT GTG TAT GAG GCC GAT GAC Leu Thr Asn Asp Cys Ser Asn Ser Ser Ile Val Tyr Glu Ala Asp Asp 65 70 75	238
GTT ATT CTG CAC ACA CCC GGC TGT GTA CCT TGT GTT CAG GAC GGT AAT Val Ile Leu His Thr Pro Gly Cys Val Pro Cys Val Gln Asp Gly Asn 80 85 90 95	286
ACA TCT GCG TGC TGG ACC CCA GTG ACA CCT ACA GTG GCA GTC AGG TAC Thr Ser Ala Cys Trp Thr Pro Val Thr Pro Thr Val Ala Val Arg Tyr $100 \hspace{1.5cm} 105 \hspace{1.5cm} 110$	334
GTC GGA GCA ACC ACC GCT TCG ATA CGC AGG CAT GTA GAC ATG TTG GTG Val Gly Ala Thr Thr Ala Ser Ile Arg Arg His Val Asp Met Leu Val 115 120 125	382
GGC GCG GCC ACG ATG TGC TCT GCT CTC TAC GTG GGT GAT ATG TGT GGG Gly Ala Ala Thr Met Cys Ser Ala Leu Tyr Val Gly Asp Met Cys Gly 130 135 140	430
GCC GTC TTC CTC GTG GGA CAA GCC TTC ACG TTC AGA CCT CGT CGC CAT Ala Val Phe Leu Val Gly Gln Ala Phe Thr Phe Arg Pro Arg Arg His 145 150 155	478
CAA ACG GTC CAG ACC TGT AAC TGC TCA CTG TAC CCA GGC CAT CTT TCA Gln Thr Val Gln Thr Cys Asn Cys Ser Leu Tyr Pro Gly His Leu Ser 160 170	526

GGA CAC CGA ATG GCT Gly His Arg Met Ala 180 541

- (2) INFORMATION FOR SEQ ID NO: 14:
 - (i) SEQUENCE CHARACTERISTICS:
 - (A) LENGTH: 180 amino acids
 - (B) TYPE: amino acid
 - (D) TOPOLOGY: linear
 - (ii) MOLECULE TYPE: protein
 - (xi) SEQUENCE DESCRIPTION: SEQ ID NO: 14:

Val Gly Ala Pro Val Gly Gly Val Ala Arg Ala Leu Ala His Gly Val 1 5 10 15

Arg Ala Leu Glu Asp Gly Ile Asn Phe Ala Thr Gly Asn Leu Pro Gly 20 25 30

Cys Ser Phe Ser Ile Phe Leu Leu Ala Leu Phe Ser Cys Leu Ile His

Pro Ala Ala Ser Leu Glu Trp Arg Asn Thr Ser Gly Leu Tyr Val Leu
50 55 60

Thr Asn Asp Cys Ser Asn Ser Ser Ile Val Tyr Glu Ala Asp Asp Val 65 70 75 80

Ile Leu His Thr Pro Gly Cys Val Pro Cys Val Gln Asp Gly Asn Thr 85 90 95

Ser Ala Cys Trp Thr Pro Val Thr Pro Thr Val Ala Val Arg Tyr Val

Gly Ala Thr Thr Ala Ser Ile Arg Arg His Val Asp Met Leu Val Gly 115 120 125

Ala Ala Thr Met Cys Ser Ala Leu Tyr Val Gly Asp Met Cys Gly Ala 130 135 140

Val Phe Leu Val Gly Gln Ala Phe Thr Phe Arg Pro Arg Arg His Gln 145 150 155 160

Thr Val Gln Thr Cys Asn Cys Ser Leu Tyr Pro Gly His Leu Ser Gly 165 170 175

His Arg Met Ala 180

- (2) INFORMATION FOR SEQ ID NO: 15:
 - (i) SEQUENCE CHARACTERISTICS:
 - (A) LENGTH: 541 base pairs
 - (B) TYPE: nucleic acid
 - (C) STRANDEDNESS: single
 - (D) TOPOLOGY: linear

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(ii) MOLECU	TLE TYPE: cDNA			
(iii) HYPOTH	ETICAL: NO			
(iii) ANTI-S	ENSE: NO			
(vii) IMMEDI (B) C	ATE SOURCE: LONE: HD10-2-14			
	E: IAME/KEY: CDS OCATION: 2541			
(xi) SEQUEN	CE DESCRIPTION:	SEQ ID NO: 15:		
			CTT GCG CAT GGC Leu Ala His Gly 15	46
			CA GGG AAT TTG CCC or Gly Asn Leu Pro 30	94
	Ser Ile Phe Le		TC TCT TGC TTA ATC ne Ser Cys Leu Ile 45	142
		Arg Asn Thr Se	CT GGC CTC TAT GTC er Gly Leu Tyr Val 60	190
		Ser Ile Val Ty	AT GAG GCC GAT GAC Fr Glu Ala Asp Asp 75	238
			T CAG GAC GGT AAT al Gln Asp Gly Asn 95	286
			NG GCA GTC AGG TAC al Ala Val Arg Tyr 110	334
			TA GAC ATA TTG GTG al Asp Ile Leu Val 125	382
		Leu Tyr Val Gl	T GAT ATG TGT GGG y Asp Met Cys Gly 140	430
			A CCT CGT CGC CAT g Pro Arg Arg His	478

CAA ACG GTC CAG ACC TGT AAC TGC TCA CTG TAC CCA GGC CAT CTT TCA

106

Gln Thr Val Gln Thr Cys Asn Cys Ser Leu Tyr Pro Gly His Leu Ser 160 165 170 170

GGA CAC CGA ATG GCT Gly His Arg Met Ala . 541

- (2) INFORMATION FOR SEQ ID NO: 16:
 - (i) SEOUENCE CHARACTERISTICS:
 - (A) LENGTH: 180 amino acids
 - (B) TYPE: amino acid (D) TOPOLOGY: linear
 - (ii) MOLECULE TYPE: protein
 - (xi) SEQUENCE DESCRIPTION: SEQ ID NO: 16:

Val Gly Ala Pro Val Gly Gly Val Ala Arg Ala Leu Ala His Gly Val

Arg Ala Leu Glu Asp Gly Ile Asn Phe Ala Thr Gly Asn Leu Pro Gly

. 20 25 30

Cys Ser Phe Ser Ile Phe Leu Pro Ala Leu Phe Ser Cys Leu Ile His 35 40 45

Pro Ala Ala Ser Leu Glu Trp Arg Asn Thr Ser Gly Leu Tyr Val Leu $50 \hspace{1cm} 55$

Thr Asn Asp Cys Ser Asn Ser Ser Ile Val Tyr Glu Ala Asp Asp Val 65 70 75 80

Ile Leu His Thr Pro Gly Cys Val Pro Cys Val Gln Asp Gly Asn Thr 85 90 95

Ser Ala Cys Trp Thr Pro Val Thr Pro Thr Val Ala Val Arg Tyr Val

Gly Ala Thr Thr Ala Ser Ile Arg Arg His Val Asp Ile Leu Val Gly
115 120 125

Ala Ala Thr Met Cys Ser Ala Leu Tyr Val Gly Asp Met Cys Gly Ala 130 135 140

Val Phe Leu Val Gly Gln Ala Phe Thr Phe Arg Pro Arg Arg His Gln 145 150 155 160

Thr Val Gln Thr Cys Asn Cys Ser Leu Tyr Pro Gly His Leu Ser Gly 165 170 175

His Arg Met Ala

- (2) INFORMATION FOR SEQ ID NO: 17 :
 - (i) SEQUENCE CHARACTERISTICS:

(A) LENGTH: 541 base pairs (B) TYPE: nucleic acid

(C) STRANDEDNESS: single (D) TOPOLOGY: linear	
(ii) MOLECULE TYPE: cDNA	
(iii) HYPOTHETICAL: NO	
(iii) ANTI-SENSE: NO	
(vii) IMMEDIATE SOURCE: (B) CLONE: HD10-2-21	
(ix) FEATURE: (A) NAME/KEY: CDS (B) LOCATION: 2541	
(xi) SEQUENCE DESCRIPTION: SEQ ID NO: 17:	
C GTC GGC GCT CCT GTA GGA GGC GTC GCA AGA GCC CTT GCG CAT GGC Val Gly Ala Pro Val Gly Gly Val Ala Arg Ala Leu Ala His Gly 1 5 10 15	46
GTG AGG GCC CTT GAA GAC GGG ATA AAT TTC GCA ACA GGG AAT TTG CCC Val Arg Ala Leu Glu Asp Gly Ile Asn Phe Ala Thr Gly Asn Leu Pro 20 25 30	94
GGT TGC TCC TTT TCT ATC TTC CTT CTT GCT CTG TTC TCT TGC TTA ATC Gly Cys Ser Phe Ser Ile Phe Leu Leu Ala Leu Phe Ser Cys Leu Ile $$35\ 40\ 45\ $	142
CAT CCA GCA GCT AGT CTA GAG TGG CGG AAC ACG TCT GGC CTC TAC GTC His Pro Ala Ala Ser Leu Glu Trp Arg Asn Thr Ser Gly Leu Tyr Val $50 \hspace{1.5cm} 55 \hspace{1.5cm} 60$	190
CTT ACC AAC GAC TGT TCC AAT AGC AGT ATT GTG TAT GAG GCC GAT GAC Leu Thr Asn Asp Cys Ser Asn Ser Ser Ile Val Tyr Glu Ala Asp Asp 65 70 75	238
GTT ATT CTG CAC ACA CCC GGC TGT GTA CCT TGT GTT CAG GAC GGT AAT Val Ile Leu His Thr Pro Gly Cys Val Pro Cys Val Gln Asp Gly Asn 80 85 90 95	286
ACA TCT GCG TGC TGG ACC CCA GTG ACA CCT ACA GTG GCA GTC AGG TAC Thr Ser Ala Cys Trp Thr Pro Val Thr Pro Thr Val Ala Val Arg Tyr $100 \hspace{1.5cm} 105 \hspace{1.5cm} 110$	334
GTC GGA GCA ACC ACC GCT TCG ATA CGC AGG CAT GTA GAC ATA TTG GTG Val Gly Ala Thr Thr Ala Ser Ile Arg Arg His Val Asp Ile Leu Val $\begin{array}{cccccccccccccccccccccccccccccccccccc$	382
GGC GCG GCC ACG ATG TGC TCT GCT CTC TAC GTG GGT GAT ATG TGT GGG Gly Ala Ala Thr Met Cys Ser Ala Leu Tyr Val Gly Asp Met Cys Gly 130 140	430

120

100 105 110

Gly Ala Thr Thr Ala Ser Ile Arg Arg His Val Asp Ile Leu Val Gly

Thr Val Gln Thr Cys Asn Cys Ser Leu Tyr Pro Gly His Leu Ser Gly

His Arg Met Ala

180													
(2) INFORMATION FOR SEQ ID NO: 19:													
(i) SEQUENCE CHARACTERISTICS: (A) LENGTH: 541 base pairs (B) TYPE: nucleic acid (C) STRANDEDNESS: single (D) TOPOLOGY: linear													
(ii) MOLECULE TYPE: cDNA													
(iii) HYPOTHETICAL: NO													
(iii) ANTI-SENSE: NO													
(vii) IMMEDIATE SOURCE: (B) CLONE: BR36-9-13													
<pre>(ix) FEATURE: (A) NAME/KEY: CDS (B) LOCATION: 2541</pre>													
(with operations programmers, one or well as													
(xi) SEQUENCE DESCRIPTION: SEQ ID NO: 19: C GTC GGC GCT CCC GTA GGA GGC GTC GCA AGA GCC CTT GCG CAT GGC	46												
Val Gly Ala Pro Val Gly Gly Val Ala Arg Ala Leu Ala His Gly 1 5 10	40												
GTG AGG GCC CTT GAA GAC GGG ATA AAT TTC GCA ACA GGG AAT TTG CCC Val Arg Ala Leu Glu Asp Gly Ile Asn Phe Ala Thr Gly Asn Leu Pro	94												
20 25 30													
GGT TGC TCC TTT TCT ATT TTC CTT CTT GCT CTG TTC TCT TGC TTA ATT Gly Cys Ser Phe Ser Ile Phe Leu Leu Ala Leu Phe Ser Cys Leu Ile	142												
35 40 45													
CAT CCA GCA GCT AGT CTA GAG TGG CGG AAT ACG TCT GGC CTC TAT GTC His Pro Ala Ala Ser Leu Glu Trp Arg Asn Thr Ser Gly Leu Tyr Val	190												
50 55 60													
CTT ACC AAC GAC TGT TCC AAT AGC AGT ATT GTG TAC GAG GCC GAT GAC Leu Thr Asn Asp Cys Ser Asn Ser Ser Ile Val Tyr Glu Ala Asp Asp	238												
65 70 75													
GTT ATT CTG CAC ACA CCC GGC TGC ATA CCT TGT GTC CAG GAC GGC AAT	286												
Val Ile Leu His Thr Pro Gly Cys Ile Pro Cys Val Gln Asp Gly Asn													
80 85 90 95													
ACA TCC ACG TGC TGG ACC CCA GTG ACA CCT ACA GTG GCA GTC AAG TAC	334												
Thr Ser Thr Cys Trp Thr Pro Val Thr Pro Thr Val Ala Val Lys Tyr 100 105 110													
GTC GGA GCA ACC ACC GCT TCG ATA CGC AGT CAT GTG GAC CTA TTA GTG	382												
Val Gly Ala Thr Thr Ala Ser Ile Arg Ser His Val Asp Leu Leu Val	382												
115 120 125													

Arg Ala Leu Glu Asp Gly Ile Asn Phe Ala Thr Gly Asn Leu Pro Gly 25 Cys Ser Phe Ser Ile Phe Leu Leu Ala Leu Phe Ser Cys Leu Ile His Pro Ala Ala Ser Leu Glu Trp Arg Asn Thr Ser Gly Leu Tyr Val Leu Thr Asn Asp Cys Ser Asn Ser Ser Ile Val Tyr Glu Ala Asp Asp Val 70 Ile Leu His Thr Pro Gly Cys Ile Pro Cys Val Gln Asp Gly Asn Thr Ser Thr Cys Trp Thr Pro Val Thr Pro Thr Val Ala Val Lys Tyr Val 100 Gly Ala Thr Thr Ala Ser Ile Arg Ser His Val Asp Leu Leu Val Gly Ala Ala Thr Met Cys Ser Ala Leu Tyr Val Gly Asp Met Cys Gly Ala 135 Val Phe Leu Val Gly Gln Ala Phe Thr Phe Arg Pro Arg Arg His Gln 150 155 Thr Val Gln Thr Cys Asn Cys Ser Leu Tyr Pro Gly His Leu Ser Gly

238

334

175

170		

His Arg 1	Wet Z	'n

HIS	Arg	met	Ala
			180

(2) INFORMATION FOR SEQ ID NO: 21:

- (i) SEQUENCE CHARACTERISTICS:
 - (A) LENGTH: 541 base pairs
 - (B) TYPE: nucleic acid
 - (C) STRANDEDNESS: single
 - (D) TOPOLOGY: linear
- (ii) MOLECULE TYPE: cDNA
- (iii) HYPOTHETICAL: NO
- (iii) ANTI-SENSE: NO
- (vii) IMMEDIATE SOURCE:
 (B) CLONE: BR36-9-20
- (ix) FEATURE:
 - (A) NAME/KEY: CDS
 - (B) LOCATION: 2..541
 - (xi) SEQUENCE DESCRIPTION: SEQ ID NO: 21:
- C GTC GGC GCT CCC GTA GGA GGC GTC GCA AGA GCC CTT GCG CAT GGC
 Val Gly Ala Pro Val Gly Gly Val Ala Arg Ala Leu Ala Hie Gly
 1 5 15
- GTG AGG GCC CTT GAA GAC GGG ATA AAT TTC GCA ACA GGG AAT TTG CCC 94 Val Arg Ala Leu Glu Asp Gly Ile Asn Phe Ala Thr Gly Asn Leu Pro 20 25 30
- GGT TGC TCC TTT TCT AFT TTC CTT CTT GCT CTG TTC TCT TGC TTA ATT
 Gly Cys Ser Phe Ser Ile Phe Leu Leu Ala Leu Phe Ser Cys Leu Ile
 45
 45
- CAT CCA GCA GCT AGT CTA GAG TGG CGG AAT ACG TCT GGC CTC TAT GTC His Pro Ala Ala Ser Leu Glu Trp Arg Asn Thr Ser Gly Leu Tyr Val $\begin{array}{c} 55 \\ 60 \end{array}$
- CTT ACC AAC GAC TGT TCC AAT AGC AGT ATT GTG TAC GAG GCC GAT GAC Leu Thr Asn Asp Cys Ser Asn Ser Ser Ile Val Tyr Glu Ala Asp Asp 65 70 75
- GTT ATT CTG CAC ACA CCC GGC TGC ATA CCT TGT GTC CAG GAC GGC AAT
 Val Ile Leu His Thr Pro Gly Cys Ile Pro Cys Val Gln Asp Gly Asn
 80 85 90 95
- ACA TCC ACG TGC TGG ACC CCA GTG ACA CCT ACA GTG GCA GTC AAG TAC
 Thr Ser Thr Cys Trp Thr Pro Val Thr Pro Thr Val Ala Val Lys Tyr
 100 105 105

WO 94/25601		112		PCT/EP94/01323							
GTC GGA GCA ACC ACC Val Gly Ala Thr Thr 115											
GGC GCG GCC ACG ATG Gly Ala Ala Thr Met 130		Leu Tyr Val									
GCT GTC TTC CTC GTG Ala Val Phe Leu Val 145											
CAA ACG GTC CAG ACC Gln Thr Val Gln Thr 160			Pro Gly His Leu								
GGA CAT CGA ATG GCT Gly His Arg Met Ala 180				541							
(2) INFORMATION FOR	SEO ID NO:	22:									
(2) INFORMATION FOR SEQ ID NO: 22: (i) SEQUENCE CHARACTERISTICS: (a) LENGTH: 180 amino acids (b) TYPE: amino acid (c) TOPOLOGY: linear (ii) MOLECULE TYPE: protein (xi) SEQUENCE DESCRIPTION: SEQ ID NO: 22:											
Val Gly Ala Pro Val	Gly Gly Val	Ala Arg Ala 10	Leu Ala His Gly 15	Val							
Arg Ala Leu Glu Asp 20	Gly Ile Asn	Phe Ala Thr 25	Gly Asn Leu Pro 30	Gly							
Cys Ser Phe Ser Ile 35	Phe Leu Leu 40	Ala Leu Phe	Ser Cys Leu Ile 45	His							
Pro Ala Ala Ser Leu 50	Glu Trp Arg 55	Asn Thr Ser	Gly Leu Tyr Val 60	Leu							
Thr Asn Asp Cys Ser 65	Asn Ser Ser 70	Ile Val Tyr 75		Val 80							
Ile Leu His Thr Pro		90	95								
Ser Thr Cys Trp Thr 100	Pro val Thr	105	110	vai							

Gly Ala Thr Thr Ala Ser Ile Arg Ser His Val Asp Leu Leu Val Gly 115 120 $^{-}$ 125

135

Val Phe Leu Val Gly Gln Ala Phe Thr Phe Arg Pro Arg Arg His Gln 145 150 150 160	
Thr Val Gln Thr Cys Asn Cys Ser Leu Tyr Pro Gly His Leu Ser Gly 165 170 175	
His Arg Met Ala 180	
(2) INFORMATION FOR SEQ ID NO: 23:	
(i) SEQUENCE CHARACTERISTICS: (A) LEMGTH: 541 base pairs (B) TYPE: nucleic acid (C) STRANDEENESS: single (D) TOPOLOGY: linear	
(ii) MOLECULE TYPE: cDNA	
(iii) HYPOTHETICAL: NO	
(iii) ANTI-SENSE: NO	
(vii) IMMEDIATE SOURCE: (B) CLONE: BR33-1-10	
(ix) FEATURE: (A) NAME/KEY: CDS (B) LOCATION: 2541	
(xi) SEQUENCE DESCRIPTION: SEQ ID NO: 23:	
C GTC GGC GCT CCC GTA GGA GGC GTC GCA AGA GCC CTT GCG CAT GGC Val Gly Ala Pro Val Gly Gly Val Ala Arg Ala Leu Ala His Gly	46

		CC CTT GCG CAT GC la Leu Ala His Gl	
	Asp Gly Ile	ACA GGG AAT TTG Thr Gly Asn Leu 30	
 		 TTC TCT TGC TTA Phe Ser Cys Leu 45	
 		 TCT GGC CTC TAT Ser Gly Leu Tyr 60	
 		 TAT GAG GCC GAT Tyr Glu Ala Asp 75	
 		GTC CAG GAC GGC Val Gln Asp Gly	

- (2) INFORMATION FOR SEQ ID NO: 24:
 - (i) SEQUENCE CHARACTERISTICS:
 - (A) LENGTH: 180 amino acids
 - (B) TYPE: amino acid (D) TOPOLOGY: linear
 - (ii) MOLECULE TYPE: protein
 - (xi) SEQUENCE DESCRIPTION: SEQ ID NO: 24:
- Val Gly Ala Pro Val Gly Gly Val Ala Arg Ala Leu Ala His Gly Val 1 5 10 15
- Arg Ala Leu Glu Asp Gly Ile Asn Phe Ala Thr Gly Asn Leu Pro Gly
- Cys Ser Phe Ser Ile Phe Leu Leu Ala Leu Phe Ser Cys Leu Ile His
- Pro Ala Ala Gly Leu Glu Trp Arg Asn Thr Ser Gly Leu Tyr Val Leu
 50 55 60
- Thr Asn Asp Cys Ser Asn Ser Ser Ile Val Tyr Glu Ala Asp Asp Val 65 70 75 80
- Ile Leu His Ala Pro Gly Cys Val Pro Cys Val Gln Asp Gly Asn Thr 85 90 95
- Ser Thr Cys Trp Thr Pro Val Thr Pro Thr Val Ala Val Arg Tyr Val
- Gly Ala Thr Thr Ala Ser Ile Arg Ser His Val Asp Leu Leu Val Gly

125

120 Ala Ala Thr Met Cys Ser Ala Leu Tyr Val Gly Asp Met Cys Gly Ala

Val Phe Leu Val Gly Gln Ala Phe Thr Phe Arg Pro Arg Arg His Gln

Thr Val Gln Thr Cys Asn Cys Ser Leu Tyr Pro Gly His Leu Ser Gly

His Arg Met Ala 180

- (2) INFORMATION FOR SEQ ID NO: 25:
 - (i) SEQUENCE CHARACTERISTICS:
 - (A) LENGTH: 541 base pairs
 - (B) TYPE: nucleic acid
 - (C) STRANDEDNESS: single (D) TOPOLOGY: linear
 - (ii) MOLECULE TYPE: cDNA
- (iii) HYPOTHETICAL: NO
 - (iii) ANTI-SENSE: NO
 - (vii) IMMEDIATE SOURCE:
 - (B) CLONE: BR33-1-19
 - (ix) FEATURE:
 - (A) NAME/KEY: CDS
 - (B) LOCATION: 2..541
 - (xi) SEQUENCE DESCRIPTION: SEQ ID NO: 25:
- C GTC GGC GCT CCC GTA GGA GGC GTC GCA AGA GCC CTT GCG CAT GGC 46 Val Gly Ala Pro Val Gly Gly Val Ala Arg Ala Leu Ala His Gly 10
- GTG AGG GCC CTT GAG GAC GGG ATA AAC TTC GCA ACA GGG AAT TTG CCC Val Arg Ala Leu Glu Asp Gly Ile Asn Phe Ala Thr Gly Asn Leu Pro 20
- GGT TGC TCT TTT TCT ATC TTC CTT CTT GCT CTG TTC TCT TGC TTA ATC Gly Cvs Ser Phe Ser Ile Phe Leu Leu Ala Leu Phe Ser Cvs Leu Ile 35
- CAT CCA GCA GCT GGT CTA GAG TGG CGG AAT ACG TCT GGC CTC TAT GTC 190 His Pro Ala Ala Gly Leu Glu Trp Arg Asn Thr Ser Gly Leu Tyr Val 50 55
- CTT ACC AAC GAC TGT TCC AAT AGT AGT ATT GTG TAT GAG GCC GAT GAC 238 Leu Thr Asn Asp Cys Ser Asn Ser Ser Ile Val Tyr Glu Ala Asp Asp 65 70

334

382

430

526

и	O 94	/2560	1				•		1	17						PCT/E	P94/01	1323
	Ser	Thr	Cys	Trp 100	Thr	Pro	Val	Thr	Pro 105	Thr	Val	Ala	Val	Arg 110	Tyr	Val		
	Gly	Ala	Thr 115	Thr	Ala	Ser	Ile	Arg 120	Ser	His	Val	Asp	Leu 125	Leu	Val	Gly		
	Ala	Ala 130	Thr	Met	Cys	Ser	Ala 135	Leu	Tyr	Val	Gly	Asp 140	Met	Cys	Gly	Ala		
	Val 145	Phe	Leu	Val	Gly	Gln 150	Ala	Phe	Thr	Phe	Arg 155	Pro	Arg	Arg	His	Gln 160		
	Thr	Val	Gln	Thr	Cys 165	Asn	Cys	Ser		Tyr 170	Pro	Gly	His	Leu	Ser 175	Gly		
	His	Arg	Met	Ala 180														
	(2)	INFO	RMAT	rion	FOR	SEQ	ID N	ю: 2	27:									
			(I (C	A) LE 3) TY C) ST 0) TO	ENGTE (PE: (RANI (POL)	HARAC H: 54 nucl DEDNE DGY:	leic ESS: line	se p ació sing ar	pairs 1	,								
	,	2221	1757		-m	AL: N	10											
				?I-SE														
	((ix)	(E FE <i>I</i> (<i>I</i>	O CL ATURE A) NA	ONE: : ME/B CATI	SOURCEY:	CDS 25	41										
			-						-									
	Va					A GG				a Ar					s Gl			46
						GAC Asp												94
			Ser			ATC Ile	Phe	Leu		Ala			ser					142

60

CAT CCA GCA GCT GGT CTA GAG TGG CGG AAT ACG TCT GGC CTC TAT GTC

His Pro Ala Ala Gly Leu Glu Trp Arg Asn Thr Ser Gly Leu Tyr Val

55

541

180 (2) INFORMATION FOR SEQ ID NO: 28:

GGA CAT CGA ATG GCT

Gly His Arg Met Ala

(i) SEQUENCE CHARACTERISTICS:

165

- (A) LENGTH: 180 amino acids (B) TYPE: amino acid
- (D) TOPOLOGY: linear
- (ii) MOLECULE TYPE: protein
- (xi) SEQUENCE DESCRIPTION: SEQ ID NO: 28:

Val Gly Ala Pro Val Gly Gly Val Ala Arg Ala Leu Ala His Gly Val 10 Arg Ala Leu Glu Asp Gly Ile Asn Phe Ala Thr Gly Asn Leu Pro Gly 25

Gln Thr Val Gln Thr Cys Asn Cys Ser Leu Tyr Pro Gly His Leu Ser

170

Cys Ser Phe Ser Ile Phe Leu Leu Ala Leu Phe Ser Cys Leu Ile His 35

Pro Ala Ala Gly Leu Glu Trp Arg Asn Thr Ser Gly Leu Tyr Val Leu

Thr Asn Asp Cys Ser Asn Ser Ser Ile Val Tyr Glu Ala Asp Asp Val 70 75

113	
Ile Leu His Ala Pro Gly Cys Val Pro Cys Val Gln Asp Gly Asn Thr 85 90 95	
Ser Thr Cys Trp Thr Pro Val Thr Pro Thr Val Ala Val Arg Tyr Val $100 \\ 105 \\ 110$	
Gly Ala Thr Thr Ala Ser Ile Arg Ser His Val Asp Leu Leu Val Gly 115 $$120$$	
Ala Ala Thr Met Cys Ser Ala Leu Tyr Val Gly Asp Met Cys Gly Ala 130 135 140	
Val Phe Leu Val Gly Gln Ala Phe Thr Phe Arg Pro Arg Arg His Gln 145 150 155 160	
Thr Val Gln Thr Cys Asn Cys Ser Leu Tyr Pro Gly His Leu Ser Gly 165 170 175	
His Arg Met Ala 180	
(2) INFORMATION FOR SEQ ID NO: 29:	
(i) SEQUENCE CHARACTERISTICS: (A) LENGTH: 287 base pairs (B) TYPE: nucleic acid (C) STRANDEDNESS: single (D) TOPOLOGY: linear (ii) MOLECULE TYPE: cDNA	
(iii) HYPOTHETICAL: NO (iii) ANTI-SENSE: NO	
(vii) IMMEDIATE SOURCE: (B) CLONE: HCCl153	
(ix) FEATURE: (A) NAME/KEY: CDS (B) LOCATION: 3287	
(xi) SEQUENCE DESCRIPTION: SEQ ID NO: 29:	
TA GAC TIT TGG GAG AGC GTC TTC ACT GGA CTA ACT CAC ATA GAT GCC ASp Phe Trp Glu Ser Val Phe Thr Gly Leu Thr His Ile asp Ala 1 $$ 5 $$ 15	47
CAC TTT CTG TCA CAG ACT AAG CAG CAG GGA CTC AAC TTC TCG TTC CTG His Phe Leu ser Gln Thr Lys Gln Gln Gly Leu Asn Phe Ser Phe Leu $20 \qquad \qquad 25 \qquad \qquad 30$	95
ACT GCC TAC CAA GCC ACT GTG TGC GCT CGC GCG CAG GCT CCT CCC CCA Thr Ala Tyr Gln Ala Thr Val Cys Ala Arg Ala Gln Ala Pro Pro Pro 35	143
AGT TGG GAC GAG ATG TGG AAG TGT CTC GTA CGG CTT AAG CCA ACA CTA	191

Ser Trp Asp Glu Met Trp Lys Cys Leu Val Arg Leu Lys Pro Thr Leu 50 55 60

CAT GGA CCT ACG CCT CTT CTA TAT CGG TTG GGG CCT GTC CAA AAT GAA . 239
His Gly Pro Thr Pro Leu Leu Tyr Arg Leu Gly Pro Val Gln Asn Glu
65 70 75

ATC TGC TTG ACA CAC CCC ATC ACA AAA TAC ATC ATG GCA TGC ATG TCA
Lle Cys Leu Thr His Pro Ile Thr Lys Tyr Ile Met Ala Cys Met Ser
80 95 95

- (2) INFORMATION FOR SEQ ID NO: 30:
 - (i) SEQUENCE CHARACTERISTICS:
 - (A) LENGTH: 95 amino acids
 - (B) TYPE: amino acid (D) TOPOLOGY: linear
 - (D) TOPOLOGI: Timear
 - (ii) MOLECULE TYPE: protein
 - (xi) SEQUENCE DESCRIPTION: SEQ ID NO: 30:

Asp Phe Trp Glu Ser Val Phe Thr Gly Leu Thr His Ile Asp Ala His 1 5 10 15

Phe Leu Ser Gln Thr Lys Gln Gln Gly Leu Asn Phe Ser Phe Leu Thr 20 25 30

Ala Tyr Gln Ala Thr Val Cys Ala Arg Ala Gln Ala Pro Pro Pro Ser 35 40 45

Trp Asp Glu Met Trp Lys Cys Leu Val Arg Leu Lys Pro Thr Leu His 50 60

Gly Pro Thr Pro Leu Leu Tyr Arg Leu Gly Pro Val Gln Asn Glu Ile 65 70 75 80

Cys Leu Thr His Pro Ile Thr Lys Tyr Ile Met Ala Cys Met Ser $85 \\ 90 \\ 95$

- (2) INFORMATION FOR SEQ ID NO: 31:
 - (i) SEQUENCE CHARACTERISTICS:
 - (A) LENGTH: 401 base pairs
 - (B) TYPE: nucleic acid
 - (C) STRANDEDNESS: single
 (D) TOPOLOGY: linear
 - (ii) MOLECULE TYPE: cDNA
 - (iii) HYPOTHETICAL: NO
 - (iii) ANTI-SENSE: NO
 - (vii) IMMEDIATE SOURCE:
 (B) CLONE: HD10-1-25

(ix) FEATURE:

(A) NAME/REY: CDS (B) LOCATION: 3401	
(xi) SEQUENCE DESCRIPTION: SEQ ID NO: 31:	
TC CAA AAT GAA ATC TGC TTG ACA CAC CCC GTC ACA AAA TAC ATT ATC Gln Asn Glu Ile Cys Leu Thr His Pro Val Thr Lys Tyr Ile Met 1 5 10	
GCA TGC ATG TCA GCT GAT CTG GAA GTA ACC ACC AGC ACC TGG GTG TT Ala Cys Met Ser Ala Asp Leu Glu Val Thr Thr Ser Thr Trp Val Le $20 \hspace{1.5cm} 25 \hspace{1.5cm} 30$	
CTT GGA GGG GTC CTC GCG GCC CTA GCG GCC TAC TGC TTG TCA GTC GG Leu Gly Gly Val Leu Ala Ala Leu Ala Ala Tyr Cys Leu Ser Val Gl 35 40	
TGC GTT GTA ATC GTG GGT CAT ATC GAG CTG GGG GGC AAG CCG GCA CT Cys Val Val Ile Val Gly His Ile Glu Leu Gly Gly Lys Pro Ala Le 50 $$50$$	
GTT CCA GAC AAG GAG GTG TTG TAT CAA CAG TAC GAT GAG ATG GAG GA Val Pro Asp Lys Glu Val Leu Tyr Gln Gln Tyr Asp Glu Met Glu Gl 65 70	
TGC TGG CAA GCC GCC CCA TAC ATC GAA CAA GCT CAG GTA ATA GCC CA Cys Ser Gln Ala Ala Pro Tyr Ile Glu Gln Ala Gln Val Ile Ala Hi 80 85 90 9	s
CAG TTC AAG GAG AAA ATC CTT GGA CTG CTG CAG CGA GCC ACC CAA CA Gln Phe Lys Glu Lys Ile Leu Gly Leu Leu Gln Arg Ala Thr Gln Gl 100 105 110	
CAA GCT GTC ATT GAG CCC GTA ATA GCT TCC AAC TGG CAA AAG CTT GA Gln Ala Val Ile Glu Pro Val Ile Ala Ser Asn Trp Gln Lys Leu Gl 125	
ACC TTC TGG CAC AAG CAT Thr Phe Trp His Lys His	401

(2) INFORMATION FOR SEQ ID NO: 32:

- (i) SEQUENCE CHARACTERISTICS:
 - (A) LENGTH: 133 amino acids
 - (B) TYPE: amino acid
 - (D) TOPOLOGY: linear
- (ii) MOLECULE TYPE: protein
- (xi) SEQUENCE DESCRIPTION: SEQ ID NO: 32:
- Gln Asn Glu Ile Cys Leu Thr His Pro Val Thr Lys Tyr Ile Met Ala 1 5 10 15

Cys	Met	Ser	Ala	Asp	Leu	Glu	Val	Thr	Thr	Ser	Thr	Trp	Val	Leu	Leu
20					25				30						

Gly Gly Val Leu Ala Ala Leu Ala Ala Tyr Cys Leu Ser Val Gly Cys 35 40 45

Val Val Ile Val Gly His Ile Glu Leu Gly Gly Lys Pro Ala Leu Val

Pro Asp Lys Glu Val Leu Tyr Gln Gln Tyr Asp Glu Met Glu Glu Cys

Ser Gln Ala Ala Pro Tyr Ile Glu Gln Ala Gln Val Ile Ala His Gln 85 90 95

Phe Lys Glu Lys Ile Leu Gly Leu Gln Arg Ala Thr Gln Gln Gln 100 105 110

Ala Val Ile Glu Pro Val Ile Ala Ser Asn Trp Gln Lys Leu Glu Thr 115 120 125 Phe Trp His Lys His 130

(2) INFORMATION FOR SEQ ID NO: 33:

- (i) SEQUENCE CHARACTERISTICS:
 - (A) LENGTH: 401 base pairs
 - (B) TYPE: nucleic acid
 - (C) STRANDEDNESS: single
 (D) TOPOLOGY: linear
- (ii) MOLECULE TYPE: CDNA
- (iii) HYPOTHETICAL: NO
- (iii) ANTI-SENSE: NO
- (vii) IMMEDIATE SOURCE:
- (B) CLONE: HD10-1-3
- (ix) FEATURE: (A) NAME/KEY: CDS
 - (B) LOCATION: 3..401
- (xi) SEQUENCE DESCRIPTION: SEQ ID NO: 33:
- TC CAA AAT GAA ATC TGC TTG ACA CAC CCC GTC ACA AAA TAC ATT ATG Gln Asn Glu Ile Cys Leu Thr His Pro Val Thr Lys Tyr Ile Met
- CTT GGA GGG GTC CTC GCG GCC CTA GCG GCC TAC TGC TTG TCA GTC GGC 143

Leu	Gly	Gly	Val 35	Leu	Ala	Ala	Leu	Ala 40	Ala	Tyr	Cys	Leu	Ser 45	Val	Gly	
						CAT His										191
						TTG Leu 70										239
						TAC Tyr										287
						CTT Leu										335
						GTA Val										383

401

(2) INFORMATION FOR SEQ ID NO: 34:

ACC TTC TGG CAC AAG CAT

Thr Phe Trp His Lys His 130

- (i) SEQUENCE CHARACTERISTICS:
 - (A) LENGTH: 133 amino acids
 - (B) TYPE: amino acid
- (D) TOPOLOGY: linear
- (ii) MOLECULE TYPE: protein
- (xi) SEQUENCE DESCRIPTION: SEQ ID NO: 34:

Gln Asn Glu Ile Cys Leu Thr His Pro Val Thr Lys Tyr Ile Met Ala 1 5 10 15

Cys Met Ser Ala Asp Leu Glu Val Thr Thr Ser Thr Trp Val Leu Leu 20 25 30

Gly Gly Val Leu Ala Ala Leu Ala Ala Tyr Cys Leu Ser Val Gly Cys
35 40 45

Val Val Ile Val Gly His Ile Glu Leu Gly Gly Lys Pro Ala Leu Val

Pro Asp Lys Glu Val Leu Tyr Gln Gln Tyr Asp Glu Met Glu Glu Cys 65 70 75 80

Ser Gln Ala Ala Pro Tyr Ile Glu Gln Ala Gln Val Ile Ala His Gln 85 90 95

Phe Lys Glu Lys Ile Leu Gly Leu Leu Gln Arg Ala Thr Gln Gln Gln

				1	24				
		100		105	i		110		
Ala	Val Ile	Glu Pro	Val Ile	Ala Ser 120	Asn Trp	Gln Lys 125		Thr	
	Trp His	Lys His							
(2)	INFORMAT	ION FOR	SEQ ID	NO: 35:					
	(A (B (C) LENGTH) TYPE:) STRANI	HARACTER H: 401 b nucleic DEDNESS: DGY: lin	ase pair acid single	s				
	(ii) MOL	ECULE TY	PE: cDN	A					
(iii) HYP	OTHETICA	L: NO						
(iii) ANT	I-SENSE:	: NO						
. (vii) IMM (B		OURCE: BR36-2	0-164					
) NAME/F) LOCATI	ON: 3		TD NO: 3	5:			
	AA AAT G In Asn G	AA ATC T	GC TTG	ACA CAC	CCC ATC	ACA AAA			47
	TGC ATG							Leu	95
	GGA GGG				Ala Tyr				143
	GTT GTG . Val Val 50						Pro Ala		191
	CCA GAC . Pro Asp :			Tyr Glr					239
	TCA CAA Ser Gln					Gln Val			287
CAG	TTC AAG	gga aaa	GTC CTT	GGA TTG	CTG CAG	CGA GCC	ACC CAA	CAA	335

Gln Phe Lys Gly Lys Val Leu Gly Leu Leu Gln Arg Ala Thr Gln Gln 100 105

CAA GCT GTC ATT GAG CCC ATA GTA ACT ACC AAC TGG CAA AAG CTT GAG 383 Gln Ala Val Ile Glu Pro Ile Val Thr Thr Asn Trp Gln Lys Leu Glu 120

GCC TTT TGG CAC AAG CAT Ala Phe Trp His Lys His 130

401

- (2) INFORMATION FOR SEQ ID NO: 36:
 - (i) SEQUENCE CHARACTERISTICS:
 - (A) LENGTH: 133 amino acids
 - (B) TYPE: amino acid
 - (D) TOPOLOGY: linear
 - (ii) MOLECULE TYPE: protein
 - (xi) SEQUENCE DESCRIPTION: SEQ ID NO: 36:

Gln Asn Glu Ile Cys Leu Thr His Pro Ile Thr Lys Tyr Ile Met Ala

Cys Met Ser Ala Asp Leu Glu Val Thr Thr Ser Thr Trp Val Leu Leu 20 25 30

Gly Gly Val Leu Ala Ala Leu Ala Ala Tyr Cys Leu Ser Val Gly Cys

Val Val Ile Val Gly His Ile Glu Leu Gly Gly Lys Pro Ala Ile Val

Pro Asp Lys Glu Val Leu Tyr Gln Gln Tyr Asp Glu Met Glu Glu Cys

Ser Gln Ala Ala Pro Tyr Ile Glu Gln Ala Gln Val Ile Ala His Gln

Phe Lys Gly Lys Val Leu Gly Leu Leu Gln Arg Ala Thr Gln Gln 100

Ala Val Ile Glu Pro Ile Val Thr Thr Asn Trp Gln Lys Leu Glu Ala 120

Phe Trp His Lys His 130

- (2) INFORMATION FOR SEQ ID NO: 37:
 - (i) SEQUENCE CHARACTERISTICS: (A) LENGTH: 401 base pairs

 - (B) TYPE: nucleic acid
 - (C) STRANDEDNESS: single
 - (D) TOPOLOGY: linear

401

126	
(ii) MOLECULE TYPE: cDNA	
(iii) HYPOTHETICAL: NO	
(iii) ANTI-SENSE: NO	•
(vii) IMMEDIATE SOURCE: (B) CLONE: BR36-20-166	
(ix) FEATURE: (A) NAME/KEY: CDS (B) LOCATION: 3401	
(xi) SEQUENCE DESCRIPTION: SEQ ID NO: 37:	
TC CAA AAT GAA ATC TGC TTG ACA CAC CCC ATC ACA AAA TAC ATC ATG Gln Asn Glu Ile Cys Leu Thr His Pro Ile Thr Lys Tyr Ile Met 1 5 10 15	47
GCA TGC ATG TCA GCT GAT CTG GAA GTA ACC ACC AGC ACC TGG GTT TTG Ala Cys Met Ser Ala Asp Leu Glu Val Thr Thr Ser Thr Trp Val Leu 20 25 30	95
CTT GGA GGG GTC CTC GCG GCC CTA GCG GCC TAC TGC TTG TCA GTC GGT Leu Gly Gly Val Leu Ala Ala Leu Ala Ala Tyr Cys Leu Ser Val Gly 35 40 45	143
TGT GTT GTG ATT GTG GGT CAT ATC GAG CTG GGG GGC AAG CCG GCA ATC Cys Val Val Ile Val Gly His Ile Glu Leu Gly Gly Lys Pro Ala Ile 50 55 60	191
GTT CCA GAC AAA GAG GTG TTG TAT CAA CAA TAC GAT GAG ATG GAA GAG Val Pro Asp Lys Glu Val Leu Tyr Gln Gln Tyr Asp Glu Met Glu Glu 65 70 75	239
TGC TCA CAA GCT GCC CCA TAT ATC GAA CAA GCT CAG GTG ATA GCT CAC Cys Ser Gln Ala Ala Pro Tyr Ile Glu Gln Ala Gln Val Ile Ala His 80 90 95	287
CAG TTC AAG GAA AAA GTC CTT GGA TTG CTG CAG CGA GCC ACC CAA CAA Gln Phe Lys Glu Lys Val Leu Gly Leu Leu Gln Arg Ala Thr Gln Gln 100 105 110	335

(2) INFORMATION FOR SEQ ID NO: 38:

115

GCC TTT TGG CAC AAG CAT Ala Phe Trp His Lys His 130

> (i) SEQUENCE CHARACTERISTICS: (A) LENGTH: 133 amino acids

CAA GCT GTC ATT GAG CCC ATA GTA ACT ACC AAC TGG CAA AAG CTT GAG

Gln Ala Val Ile Glu Pro Ile Val Thr Thr Asn Trp Gln Lys Leu Glu

- (B) TYPE: amino acid
- (D) TOPOLOGY: linear
- (ii) MOLECULE TYPE: protein
- (xi) SEQUENCE DESCRIPTION: SEQ ID NO: 38:
- Gln Asn Glu Ile Cys Leu Thr His Pro Ile Thr Lys Tyr Ile Met Ala 1 5 10 15
- Cys Met Ser Ala Asp Leu Glu Val Thr Thr Ser Thr Trp Val Leu Leu 20 25 30
- Gly Gly Val Leu Ala Ala Leu Ala Ala Tyr Cys Leu Ser Val Gly Cys $35 \hspace{1cm} 40 \hspace{1cm} 45 \hspace{1cm}$
- Val Val Ile Val Gly His Ile Glu Leu Gly Gly Lys Pro Ala Ile Val 50 55 60
- Pro Asp Lys Glu Val Leu Tyr Gln Gln Tyr Asp Glu Met Glu Glu Cys 65 70 75 80
- Ser Gln Ala Ala Pro Tyr Ile Glu Gln Ala Gln Val Ile Ala His Gln
 . 85 90 95
- Phe Lys Glu Lys Val Leu Gly Leu Gln Arg Ala Thr Gln Gln Gln 100 105 110
- Ala Val Ile Glu Pro Ile Val Thr Thr Asn Trp Gln Lys Leu Glu Ala 115 120 125

Phe Trp His Lys His

- (2) INFORMATION FOR SEQ ID NO: 39:
 - (i) SEQUENCE CHARACTERISTICS:
 - (A) LENGTH: 401 base pairs
 - (B) TYPE: nucleic acid
 - (C) STRANDEDNESS: single (D) TOPOLOGY: linear
 - (ii) MOLECULE TYPE: cDNA
 - (iii) HYPOTHETICAL: NO
 - (iii) ANTI-SENSE: NO
 - (vii) IMMEDIATE SOURCE:
 - (B) CLONE: BR36-20-165
 - (ix) FEATURE:
 - (A) NAME/KEY: CDS
 - (B) LOCATION: 3..401
 - (xi) SEQUENCE DESCRIPTION: SEQ ID NO: 39:

		GAA . Glu											47
			Asp				Thr					TTG Leu	95
						Ala					Val	GGT Gly	143
		Ile			Glu					Pro		ATC	191
	Asp								Glu			GAG Glu	239
								Gln				CAC His 95	287
							Gln					CAA Gln	335
						Thr						GAG Glu	383
		CAC His											401

- (2) INFORMATION FOR SEQ ID NO: 40:
 - (i) SEQUENCE CHARACTERISTICS:
 - (A) LENGTH: 133 amino acids
 - (B) TYPE: amino acid
 - (D) TOPOLOGY: linear
 - (ii) MOLECULE TYPE: protein
 - (xi) SEQUENCE DESCRIPTION: SEQ ID NO: 40:

Gln Asn Glu Ile Cys Leu Thr His Pro Ile Thr Lys Tyr Ile Met Ala 1 5 10 15.

Cys Met Ser Ala Asp Leu Glu Val Thr Thr Ser Thr Trp Val Leu Leu 20 25 30

Gly Gly Val Leu Ala Ala Leu Ala Ala Tyr Cys Leu Ser Val Gly Cys $35 \hspace{1cm} 40 \hspace{1cm} 45$

50 55 60	
Pro Asp Lys Glu Val Leu Tyr Gln Gln Tyr Asp Glu Met Glu Glu Cys 65 70 75 80	
Ser Gln Ala Ala Pro Tyr Ile Glu Gln Ala Gln Val Ile Ala His Gln 85 90 95	
Phe Lys Glu Lys Val Leu Gly Leu Leu Gln Arg Ala Thr Gln Gln 100 105 110	
Ala Val Ile Glu Pro Ile Val Thr Thr Asn Trp Gln Lys Leu Glu Ala 115 120 125	
Phe Trp His Lys His 130	
(2) INFORMATION FOR SEQ ID NO: 41:	
(i) SEQUENCE CHARACTERISTICS: (A) LENGTH: 509 base pairs (B) TYPE: nucleic acid (C) STRANDEDNESS: single (D) TOPOLOGY: linear	
(ii) MOLECULE TYPE: cDNA	
(iii) HYPOTHETICAL: NO	
(iii) ANTI-SENSE: NO	
(vii) IMMEDIATE SOURCE: (B) CLONE: PC-2-1	
(ix) FEATURE: (A) NAME/KEY: CDS	
(B) LOCATION: 3509	
(xi) SEQUENCE DESCRIPTION: SEQ ID NO: 41:	
CC ATG AGC ACG AAT CCT AAA CCT CAA AGA AAA ACC AAA AGA AAC ACC	47
Met Ser Thr Asn Pro Lys Pro Gln Arg Lys Thr Lys Arg Asn Thr 1 5 10 15	*/
AAC CGT CGC CCA CAG GAC GTC AAG TTC CCG GGC GGT GGT CAG ATC GTT Asn Arg Arg Pro Gln Asp Val Lys Phe Pro Gly Gly Gly Gln Ile Val 20 25 30	95
GGC GGA GTT TAC TTG TTG CCG CGC AGG GGC CCT AGG ATG GGT GTG CGC Gly Gly Val Tyr Leu Leu Pro Arg Arg Gly Pro Arg Met Gly Val Arg 35 40 45	143

GCG ACT CGG AAG ACT TCG GAA CGG TCG CAA CCC CGT GGA CGG CGT CAG

Ala Thr Arg Lys Thr Ser Glu Arg Ser Gln Pro Arg Gly Arg Arg Gln

		50			55			60		
			GCG Ala							239
			CCC Pro							287
	 		 CCT Pro 100	 		 	 			335
			TCG Ser							383
			gat Asp							431
			GCA Ala							479
-	 		 TAT Tyr							509

- (2) INFORMATION FOR SEQ ID NO: 42:
 - (i) SEQUENCE CHARACTERISTICS:
 - (A) LENGTH: 169 amino acids
 - (B) TYPE: amino acid
 (D) TOPOLOGY: linear
 - (ii) MOLECULE TYPE: protein
 - (xi) SEQUENCE DESCRIPTION: SEQ ID NO: 42:

Met Ser Thr Asn Pro Lys Pro Gln Arg Lys Thr Lys Arg Asn Thr Asn

Arg Arg Pro Gln Asp Val Lys Phe Pro Gly Gly Gly Gln Ile Val Gly
20 25 30

Gly Val Tyr Leu Leu Pro Arg Arg Gly Pro Arg Met Gly Val Arg Ala

Thr Arg Lys Thr Ser Glu Arg Ser Gln Pro Arg Gly Arg Arg Gln Pro 50 55 60

Ile Pro Lys Ala Arg Gln Pro Thr Gly Arg Ser Trp Gly Gln Pro Gly 65 70 75 80

Tyr Pro Trp Pro Leu Tyr Ala Asn Glu Gly Leu Gly Trp Ala Gly Trp

									31							
				85					90					95		
Le	ı Let	ı Ser	100		Gly	Ser	Arg	Pro 105	Asn	Trp	Gly	Pro	Asn 110	Asp	Pro	
Arg	Arg	115	Ser	Arg	Asn	Leu	Gly 120	Lys	Val	Ile	Asp	Thr 125	Leu	Thr	Cys	
Gl	130		Asp	Leu	Met	Gly 135	Tyr	Ile	Pro	Leu	Val 140	Gly	Gly	Pro	Ile	
Gl ₃ 145		Val	Ala	Arg	Ala 150		Ala	His	Gly	Val 155	Arg	Val	Leu	Glu	Asp 160	
Gly	val	Asn	Tyr	Ala 165	Thr	Gly	Asn	Leu								
(2)	INF	ORMA	TION	FOR	SEQ	ID I	IO:4:	3:								
, ,	(i	(. (:	QUENC A) LI B) TI C) SI D) TO	engti Ype : Prani	nuci DEDNI	09 ba leic ESS:	ase p acid	pair:	8							
	(ii) MO	LECUI	LE T	PE:	CDNZ										
	(iii) HY	POTHE	TIC	L: 1	10										
	(iii) AN	TI-SE	ENSE	NO											
		(1	MEDIA B) CI	ONE												
	(1X	()	ATURE A) NA B) LC	ME/E			609									
	(xi) SE(QUENC	E DE	SCRI	PTIC	N: S	EQ I	D NO	: 43	:					
			ACG A						rg L							47
			CCA Pro													95
			TAC Tyr 35													143
			AAG Lys													191

WO 94	/2560	1						13	32						PCT/EI	294/01323
							Pro								CCC Pro	239
								AAT Asn							GGG Gly 95	287
								CGG Arg								335
								GGT Gly 120							ACG Thr	383
	Gly							TAT Tyr								431
								GCA Ala							GAG Glu	479
								AAT Asn								509
(2)		(i) S	EQUE	ence Engti	CHAI		RIS:	i4: TICS: acid								
						line										
						prot										
	(xi)	SEÇ	UENC	E DE	SCR	PTIC	ON: S	SEQ 1	ID NO	0: 44	١:					
Met 1	Ser	Thr	Asn	Pro 5	Lys	Pro	Gln	Arg	Lys 10	Thr	Lys	Arg	Asn	Thr 15	Asn	
Arg	Arg	Pro	Gln 20	qaA	Val	Lys	Phe	Pro 25	Gly	Gly	Gly	Gln	Ile 30	Val	Gly	
Gly	Val	Tyr 35	Leu	Leu	Pro	Arg	Arg 40	Gly	Pro	Arg	Met	Gly 45	Val	Arg	Ala	
Thr	Arg 50	Lys	Thr	Ser	Glu	Arg 55	Ser	Gln	Pro	Arg	Gly 60	Arg	Arg	Gln	Pro	
Ile 65	Pro	Lys	Ala	Arg	Gln 70	Pro	Thr	Gly	Arg	Ser 75	Trp	Gly	Gln	Pro	Gly 80	
Tyr	Pro	Trp	Pro	Leu 85	Tyr	Ala	Asn	Glu	Gly 90	Leu	Gly	Trp	Ala	Gly 95	Trp	

								1	133								
Let	ı Lev	Ser	Pro 100		Gly	Ser	Arg	Pro 105		Trp	Gly	Pro	Asn 110		Pro		
Arg	Arg	Lys 115		Arg	Asn	Leu	Gly 120		Val	Ile	Asp	Thr 125		Thr	Cys		
Gly	Phe 130	Ala	Asp	Leu	Met	Gly 135		Ile	Pro	Leu	Val 140		Gly	Pro	Ile		
Gly 145	Gly	Val	Ala	Arg	Ala 150		Ala	His	Gly	Val 155	Arg	Val	Leu	Glu	Asp 160		
Gly	Val	Asn	Tyr	Ala 165	Thr	Gly	Asn	Leu									
(2)	INF	ORMA!	rion	FOR	SEQ	ID I	NO:	45:									
	(i	(1	QUENC A) Li B) Ti C) Si O) To	engt: Pe: Pran	H: 5 nuc DEDN	80 b leic ESS:	ase aci sin	pair d	s								
	(ii	MOI	LECUI	E T	YPE:	cDN	Α.										
	(iii	HYI	POTHE	TIC	AL: 1	NO											
	(111)	ANT	TI-SE	INSE	: NO												
	(vii	IMI (E	EDIA 3) CI														
	(ix)		TURE L) NA B) LC	ME/I			580										
	(xi)	SEC	UENC	E DI	SCR	PTIC	N: 8	SEQ 1	D NO): 45	:						
		GC GG 78 Gl							у Ту					1 G1			46
		ATT Ile															94
		GAC Asp														1	42
		ATC Ile 50														1	90
TCT	GCA	GTT	ccc	TAC	CGA	AAT	GCC	TCT	GGG	ATT	TAT	CAT	GTT	ACC	AAT	2	38

								-								
Ser	Ala 65	Val	Pro	Tyr	Arg	Asn 70	Ala	Ser	Gly	Ile	Tyr 75	His	Val	Thr	Asn	
	TGC Cys														CTA Leu 95	286
	GCA Ala															334
	TGG Trp															382
	ACG Thr															430
	CTC Leu 145															478
	GTA Val															526
	AAC Asn															574
ATG Met																580

- (2) INFORMATION FOR SEQ ID NO: 46:
 - (i) SEQUENCE CHARACTERISTICS:
 - (A) LENGTH: 193 amino acids
 - (B) TYPE: amino acid
 - (D) TOPOLOGY: linear
 - (ii) MOLECULE TYPE: protein
 - (xi) SEQUENCE DESCRIPTION: SEQ ID NO: 46:

Thr Cys Gly Phe Ala Asp Leu Met Gly Tyr Ile Pro Leu Val Gly Gly 1 15

Pro Ile Gly Gly Val Ala Arg Ala Leu Ala His Gly Val Arg Val Leu

Glu Asp Gly Val Asn Tyr Ala Thr Gly Asn Leu Pro Gly Cys Ser Phe 35 45

Ser Ile Phe Ile Leu Ala Leu Leu Ser Cys Leu Thr Val Pro Ala Ser 50 55

Ala Val Pro Tyr Arg Asn Ala Ser Gly Ile Tyr His Val Thr Asn Asp 65 70 75 80

Cys Pro Asn Ser Ser Ile Val Tyr Glu Ala Asp Asn Leu Ile Leu His 85 90 95

Ala Pro Gly Cys Val Pro Cys Val Met Thr Gly Asn Val Ser Arg Cys 100 105 110

Trp Val Gln Ile Thr Pro Thr Leu Ser Ala Pro Ser Leu Gly Ala Val 115 120 125

Thr Ala Pro Leu Arg Arg Ala Val Asp Tyr Leu Ala Gly Gly Ala Ala 130 135 140

Val Gly Gln Met Phe Thr Tyr Arg Pro Arg Gln His Ala Thr Val Gln 165 170 175

Asn Cys Asn Cys Ser Ile Tyr Ser Gly His Val Thr Gly His Arg Met 180 185 190

Ala

- (2) INFORMATION FOR SEQ ID .NO: 47:
 - (i) SEQUENCE CHARACTERISTICS:
 - (A) LENGTH: 580 base pairs
 - (B) TYPE: nucleic acid
 - (C) STRANDEDNESS: single
 (D) TOPOLOGY: linear
 - (ii) MOLECULE TYPE: cDNA
 - (iii) HYPOTHETICAL: NO
 - (iii) ANTI-SENSE: NO
 - (vii) IMMEDIATE SOURCE:
 - (B) CLONE: PC-4-6
 - (ix) FEATURE: (A) NAME/KEY: CDS (B) LOCATION: 2..580
 - (xi) SEQUENCE DESCRIPTION: SEQ ID NO: 47:
- A ACG TGC GGA TTC GCC GAT CTC ATG GGG TAT ATC CCG CTC GTA GGC Thr Cys Gly Phe Ala Asp Leu Met Gly Tyr Ile Pro Leu Val Gly 1 5 10
- GGC CCC ATT GGG GGC GTC GCA AGG GCT CTC GCA CAC GGT GTG AGG GTC

(2) INFORMATION FOR SEO ID NO: 48:

ATG GCA

Met Ala

- (i) SEQUENCE CHARACTERISTICS: (A) LENGTH: 193 amino acids
 - (B) TYPE: amino acid
 - (D) TOPOLOGY: linear
- (ii) MOLECULE TYPE: protein
- (xi) SEQUENCE DESCRIPTION: SEO ID NO: 48:

WO 94/25601 PCT/EP94/01323 137

Thr Cys Gly Phe Ala Asp Leu Met Gly Tyr Ile Pro Leu Val Gly Gly

Pro Ile Gly Gly Val Ala Arg Ala Leu Ala His Gly Val Arg Val Leu

Glu Asp Gly Val Asn Tyr Ala Thr Gly Asn Leu Pro Gly Cys Ser Phe

Ser Ile Phe Ile Leu Ala Leu Leu Ser Cys Leu Thr Val Pro Ala Ser

Ala Val Pro Tyr Arg Asn Ala Ser Gly Ile Tyr His Val Thr Asn Asp

Cys Pro Asn Ser Ser Ile Val Tyr Glu Ala Asp Asn Leu Ile Leu His

Ala Pro Gly Cys Val Pro Cys Val Met Thr Gly Asn Val Ser Arg Cys 105

Trp Val Gln Ile Thr Pro Thr Leu Ser Ala Pro Ser Leu Gly Ala Val 120

Thr Ala Pro Leu Arg Arg Ala Val Asp Tyr Leu Ala Gly Gly Ala Ala

Leu Cys Ser Ala Leu Tyr Val Gly Asp Ala Cys Gly Ala Leu Phe Leu 145

Val Gly Gln Met Phe Thr Tyr Arg Pro Arg Gln His Ala Thr Val Gln

Asn Cys Asn Cys Ser Ile Tyr Ser Gly His Val Thr Gly His Arg Met 185

Ala

- (2) INFORMATION FOR SEO ID NO: 49:
 - (i) SEOUENCE CHARACTERISTICS: (A) LENGTH: 959 base pairs
 - (B) TYPE: nucleic acid
 - (C) STRANDEDNESS: single
 - (D) TOPOLOGY: linear
 - (ii) MOLECULE TYPE: cDNA
 - (iii) HYPOTHETICAL: NO
 - (iii) ANTI-SENSE: NO
 - (vii) IMMEDIATE SOURCE: (B) CLONE: PC-3-4

(ix) FEATURE:

(A) NAME/KEY: CDS (B) LOCATION: 3..959

(xi) SEQUENCE DESCRIPTION: SEQ ID NO: 49:	
CC ATG AGC ACG AAT CCT AAA CCT CAA AGA AAA ACC AAA AGA AAC A Met Ser Thr Asn Pro Lys Pro Gln Arg Lys Thr Lys Arg Asn T 1	
AAC COT COC CCA CAG GAC GTC AAG TTC CCG GGC GGT GGT CAG ATC CAS ATG	
GGC GGA GTT TAC TTG TTG CCG CGC AGG GGC CCT AGG ATG GGT GTG GGL GDly Gly Val Tyr Leu Leu Pro Arg Arg Gly Pro Arg Met Gly Val 2 35 40 45	
GCG ACT CGG AAG ACT TCG GAA CGG TCG CAA CCC CGT GGA CGG CGT (Ala Thr Arg Lys Thr Ser Glu Arg Ser Gln Pro Arg Gly Arg Arg (50 55 60	
CCT ATT CCC AAG GGG CGC CAG CCC ACG GGC CGG TCC TGG GGT CAA C Pro Ile Pro Lys Ala Arg Gln Pro Thr Gly Arg Ser Trp Gly Gln I 65 70 75	
GGG TAC CCT TGG CCC CTT TAC GCC AAT GAG GGC CTC GGG TGG GCA GGly Tyr Pro Trp Pro Leu Tyr Ala Asn Glu Gly Leu Gly Trp Ala G	
TGG CTG CTC CCC CGA GGC TCT CGG CCT AAT TGG GGC CCC AAT CTC CGC Leu Leu Ser Pro Arg Gly Ser Arg Pro Asn Trp Gly Pro Asn I 100 105 110	
CCC CGG CGA ARA TCG CGT ART TTG GGT ARG GTC ATC GAT ACC CTA A Pro Arg Arg Lys Ser Arg Asn Leu Gly Lys Val Ile Asp Thr Leu T 115 120 125	
TGC GGA TTC GCC GAT CTC ATG GGG TAT ATC CCG CTC GTA GGC GGC C Cys Gly Phe Ala Asp Leu Met Gly Tyr Ile Pro Leu Val Gly Gly F 130 135 140	
ATT GGG GGC GTC GCA AGG GCT CTC GCA CAC GGT GTG AGG GTC CTT G Ile Gly Gly Val Ala Arg Ala Leu Ala His Gly Val Arg Val Leu G 145 150	
GAC GGG GTA AAC TAT GCA ACA GGG AAT TTA CCC GGT TGC TCT TTC TASD Gly Val Asn Tyr Ala Thr Gly Asn Leu Pro Gly Cys Ser Phe S 160 165 170 1	
ATC TTT ATT CTT GCT CTT CTC TCG TGT CTG ACC GTT CCG GCC TCT G Ile Phe Ile Leu Ala Leu Leu Ser Cys Leu Thr Val Pro Ala Ser A 180 185 190	
GTT CCC TAC CGA AAT GCC TCT GGG ATT TAT CAT GTT ACC AAT GAT T Val Pro Tyr Arg Asn Ala Ser Gly Ile Tyr His Val Thr Asn Asp C 195 200 205	

CCA AAC TCT TCC ATA GTC TAT GAG GCA GAT AAC CTG ATC CTA CAC GCA

Pro	Asn	Ser	Ser	Ile	val	Tyr	Glu	Ala	Asp	Asn	Leu	Ile	Leu	His	Ala	
		210					215					220				
CCT	GGT	TGC	GTG	CCT	TGT	GTC	ATG	ACA	GGT	AAT	GTG	AGT	AGA	TGC	TGG	719
Pro	Gly	Cys	Val	Pro	Cys	Val	Met	Thr	Gly	Asn	Val	Ser	Arg	Cys	Trp	
	225					230					235					
GTC	CAA	ATT	ACC	CCT	ACA	CTG	TCA	GCC	CCG	AGC	CTC	GGA	GCA	GTC	ACG	767
Val	Gln	Ile	Thr	Pro	Thr	Leu	Ser	Ala	Pro	Ser	Leu	Gly	Ala	Val	Thr	
240					245					250					2 5 5	
GCT	CCT	CTT	CGG	AGA	GCC	GTT	GAC	TAC	CTA	GCG	GGA	GGG	GCT	GCC	CTC	815
Ala	Pro	Leu	Arg	Arg	Ala	Val	Asp	Tyr	Leu	Ala	Gly	Gly	Ala	Ala	Leu	
				260					265					270		
TGC	TCC	GCG	TTA	TAC	GTA	GGA	GAC	GCG	TGT	GGG	GCA	CTA	TTC	TTG	GTA	863
Cys	Ser	Ala	Leu	Tyr	Val	Gly	Asp	Ala	Cys	Gly	Ala	Leu	Phe	Leu	Val	
			275					280					285			
	CAA															911
Gly	Gln	Met	Phe	Thr	Tyr	Arg	Pro	Arg	Gln	His	Ala	Thr	Val	Gln	Asn	
		290					295					300				
	AAC															959
Cys	Asn	Сув	Ser	Ile	Tyr		Gly	His	Val	Thr		His	Arg	Met	Ala	
	305					310					315					
(2)	INFO	DRMAT	MOI	FOR	SEQ	ID N	10: 5	:0:								
				NCE												
				NGTI				acıc	s							
				PE:												
		(I) TC	POLC	GY:	line	ar									
	/441	MOT	TOTAL	m ms	mm.											
	(11)	MOL	TEC UI	E TY	PE:	proc	em									
	(xi)	SEC	UENC	E DE	SCRI	PTIC	N: 8	EQ I	D NO	: 50	:					
	Ser	Thr	Asn		Lys	Pro	Gln	Arg		Thr	Lys	Arg	Asn		Asn	
1				5					10					15		
Arg	Arg	Pro		Asp	Val	Lys	Phe		Gly	GIA	GLY	GIn		Val	Gly	
			20					25					30			

Gly Val Tyr Leu Leu Pro Arg Arg Gly Pro Arg Met Gly Val Arg Ala

Thr Arg Lys Thr Ser Glu Arg Ser Gln Pro Arg Gly Arg Arg Gln Pro 50 55 60

Ile Pro Lys Ala Arg Gln Pro Thr Gly Arg Ser Trp Gly Gln Pro Gly

Tyr Pro Trp Pro Leu Tyr Ala Asn Glu Gly Leu Gly Trp Ala Gly Trp

35

85

Leu Leu Ser Pro Arg Gly Ser Arg Pro Asn Trp Gly Pro Asn Asp Pro

Arg Arg Lys Ser Arg Asn Leu Gly Lys Val Ile Asp Thr Leu Thr Cys 115 120 125

- Gly Phe Ala Asp Leu Met Gly Tyr Ile Pro Leu Val Gly Gly Pro Ile 130 135 140
- Gly Gly Val Ala Arg Ala Leu Ala His Gly Val Arg Val Leu Glu Asp 145 150 155 160
- Gly Val Asn Tyr Ala Thr Gly Asn Leu Pro Gly Cys Ser Phe Ser Ile 165 170 175
- Phe Ile Leu Ala Leu Leu Ser Cys Leu Thr Val Pro Ala Ser Ala Val 180 185 190
- Pro Tyr Arg Asn Ala Ser Gly Ile Tyr His Val Thr Asn Asp Cys Pro 195 200 205
- Asn Ser Ser Ile Val Tyr Glu Ala Asp Asn Leu Ile Leu His Ala Pro 210 215 220
- Gly Cys Val Pro Cys Val Met Thr Gly Asn Val Ser Arg Cys Trp Val 225 230 235
- Gln Ile Thr Pro Thr Leu Ser Ala Pro Ser Leu Gly Ala Val Thr Ala 245 250 255
- Pro Leu Arg Arg Ala Val Asp Tyr Leu Ala Gly Gly Ala Ala Leu Cys 260 265 270
- Ser Ala Leu Tyr Val Gly Asp Ala Cys Gly Ala Leu Phe Leu Val Gly 275 280 285
- Gln Met Phe Thr Tyr Arg Pro Arg Gln His Ala Thr Val Gln Asn Cys 290 295 300
- Asn Cys Ser Ile Tyr Ser Gly His Val Thr Gly His Arg Met Ala 305 310 315
- (2) INFORMATION FOR SEQ ID NO: 51:
 - (i) SEQUENCE CHARACTERISTICS:
 - (A) LENGTH: 959 base pairs
 - (B) TYPE: nucleic acid
 - (C) STRANDEDNESS: single
 - (D) TOPOLOGY: linear
 - (ii) MOLECULE TYPE: cDNA
 - (iii) HYPOTHETICAL: NO
 - (iii) ANTI-SENSE: NO
 - (vii) IMMEDIATE SOURCE:

(B) CLONE: PC-3-8

(ix) FEATURE: (A) NAME/KEY: CDS (B) LOCATION: 3..959

	(xi) SE	QUEN	CE D	ESCR	IPTI	ON:	SEQ	ID N	iO: 5	51:					
								CAA Gln								47
					Asp					Gly					GTT Val	95
				Leu					Gly					Val	CGC Arg	143
			Lys					Ser					Arg		CAG Gln	191
		Pro					Pro					Trp			CCC Pro	239
	Тух					Tyr					Leu				GGG Gly 95	287
					Arg					Asn					GAC Asp	335
				Ser											ACG Thr	383
								Tyr					Gly		CCC Pro	431
							Leu	GCA Ala				Arg			GAG Glu	479
								AAT Asn			Gly				TCT Ser 175	527
								-TGT Cys							GCA Ala	575
GTT	ccc	TAC	CGA	AAT	GCC	TCT	GGG	ATT	TAT	CAT	GTT	ACC	AAT	GAT	TGC	623

									-							
Va	l Pro	Tyr	Arg 195	Asn	Ala	Ser	Gly	11e 200	Tyr	His	Val	Thr	Asn 205	Asp	Cys	
	A AAC o Asn															671
	T GGT o Gly 225															719
	C CAA 1 Gln 0															767
	T CCT a Pro															815
	C TCC s Ser															863
	C CAA y Gln															911
	C AAC s Asn 305															959
(2) INF	ORMA:	rion	FOR	SEQ	ID 1	10: !	52:								

- (i) SEQUENCE CHARACTERISTICS:
 - (A) LENGTH: 319 amino acids
 - (B) TYPE: amino acid
 - (D) TOPOLOGY: linear
- (ii) MOLECULE TYPE: protein
- (xi) SEQUENCE DESCRIPTION: SEQ ID NO: 52:

Met Ser Thr Asn Pro Lys Pro Gln Arg Lys Thr Lys Arg Asn Thr Asn 1 $$ 5 $$ 10 $$ 15

Arg Arg Pro Gln Asp Val Lys Phe Pro Gly Gly Gly Gln Ile Val Gly 20 25 30

Gly Val Tyr Leu Leu Pro Arg Arg Gly Pro Arg Met Gly Val Arg Ala 35 40 45

Thr Arg Lys Thr Ser Glu Arg Ser Gln Pro Arg Gly Arg Arg Gln Pro 50 60

Ile Pro Lys Ala Arg Gln Pro Thr Gly Arg Ser Trp Gly Gln Pro Gly 65 70 75 80

Tyr Pro Trp Pro Leu Tyr Ala Asn Glu Gly Leu Gly Trp Ala Gly Trp

Leu Leu Ser Pro Arg Gly Ser Arg Pro Asn Trp Gly Pro Asn Asp Pro 100 105

Arg Arg Lys Ser Arg Asn Leu Gly Lys Val Ile Asp Thr Leu Thr Cys

Gly Phe Ala Asp Leu Met Gly Tyr Ile Pro Leu Val Gly Gly Pro Val

Gly Gly Val Ala Arg Ala Leu Ala His Gly Val Arg Val Leu Glu Asp

Gly Val Asn Tyr Pro Thr Gly Asn Leu Pro Gly Cys Ser Phe Ser Ile 170

Phe Ile Leu Ala Leu Leu Ser Cys Leu Thr Val Pro Ala Ser Ala Val

Pro Tyr Arg Asn Ala Ser Gly Ile Tyr His Val Thr Asn Asp Cys Pro 200

Asn Ser Ser Ile Val Tyr Glu Ala Asp Asn Leu Ile Leu His Ala Pro

Gly Cys Val Pro Cys Val Met Thr Gly Asn Val Ser Arg Cys Trp Val 230 235

Gln Ile Thr Pro Thr Leu Ser Ala Pro Ser Leu Gly Ala Val Thr Ala 245

Pro Leu Arg Arg Ala Val Asp Tyr Leu Ala Gly Gly Ala Ala Leu Cys 265

Ser Ala Leu Tyr Val Gly Asp Ala Cys Gly Ala Leu Phe Leu Val Gly

Gln Met Phe Thr Tyr Arg Pro Arg Gln His Ala Thr Val Gln Asn Cys

Asn Cys Ser Ile Tyr Ser Gly His Val Thr Gly His Arg Met Ala

- (2) INFORMATION FOR SEQ ID NO: 53:
 - (i) SEQUENCE CHARACTERISTICS:
 - (A) LENGTH: 959 base pairs (B) TYPE: nucleic acid

 - (C) STRANDEDNESS: single (D) TOPOLOGY: linear
 - (ii) MOLECULE TYPE: cDNA
 - (iii) HYPOTHETICAL: NO

(1111)	ANTI-SENSE:	NO

(vii)	IMMEI	DIATE	S	OUR	Œ:	
	(B)	CLOM	٠.	PC	C/E	:1

(ix) FEATURE:

(A) NAME/KEY: CDS (B) LOCATION: 2..959

(xi) SEQUENCE DESCRIPTION: SEQ ID NO: 53:

CCATGAGCAC GAATCCTAAA CCTCAAAGAA AAACCAAAAG AAACACCAAC CGTCGCCCAC 60 AGGACGTCAA GTTCCCGGGC GGTGGTCAGA TCGTTGGCGG AGTTTACTTG TTGCCGCGCA 120 GGGGCCCTAG GATGGGTGTG CGCGCGACTC GGAAGACTTC GGAACGGTCG CAACCCCGTG 180 GACGGCGTCA GCCTATTCCC AAGGCGCGCC AGCCCACGGG CCGGTCCTGG GGTCAACCCG 240 GGTACCCTTG GCCCCTTTAC GCCAATGAGG GCCTCGGGTG GGCAGGGTGG CTGCTCTCCC 300 CTCGAGGCTC TCGGCCTAAT TGGGGCCCCA ATGACCCCCG GCGAAAATCG CGTAATTTGG 360 GTARGGTCAT CGATACCCTA ACGTGCGGAT TCGCCGATCT CATGGGGTAY ATCCCGCTCG 420 TAGGCGGCCC CRTTGGGGGC GTCGCAAGGG CTCTCGCACA CGGTGTGAGG GTCCTTGAGG 480 ACGGGGTAAA CTATSCAACA GGGAATTTAC CCGGTTGCTC TTTCTCTATC TTTATTCTTG 540 CTCTTCTCTC GTGTCTGACC GTTCCGGCCT CTGCAGTTCC CTACCGAAAT GCCTCTGGGA 600 TTTATCATGT TACCAATGAT TGCCCAAACT CTTCCATAGT CTATGAGGCA GATAACCTGA 660 TCCTACACGC ACCTGGTTGC GTGCCTTGTG TCATGACAGG TAATGTGAGT AGATGCTGGG 720 TCCAAATTAC CCCTACACTG TCAGCCCCGA GCCTCGGAGC AGTCACGGCT CCTCTTCGGA 780 GAGCCGTTGA CTACCTAGCG GGAGGGGCTG CCCTCTGCTC CGCGTTATAC GTAGGAGACG 840 CGTGTGGGGC ACTATTCTTG GTAGGCCAAA TGTTCACCTA TAGGCCTCGC CAGCACGCTA 900 CGGTGCAGAA CTGCAACTGT TCCATTTACA GTGGCCATGT TACCGGCCAC CGGATGGCA 959

(2) INFORMATION FOR SEO ID NO: 54:

- (i) SEQUENCE CHARACTERISTICS:
 - (A) LENGTH: 319 amino acids (B) TYPE: amino acid
 - (D) TOPOLOGY: linear
- (ii) MOLECULE TYPE: protein
- (xi) SEQUENCE DESCRIPTION: SEQ ID NO: 54:

Met Ser Thr Asn Pro Lys Pro Gln Arg Lys Thr Lys Arg Asn Thr Asn 1 5 10 15

Arg Arg	Pro Gln	Asp	Val	Lys	Phe	Pro	Gly	Gly	Gly	Gln	Ile	Val	Gly
	20					25					30		

- Gly Val Tyr Leu Leu Pro Arg Arg Gly Pro Arg Met Gly Val Arg Ala 35 \$40\$
- Thr Arg Lys Thr Ser Glu Arg Ser Gln Pro Arg Gly Arg Arg Gln Pro 50
- Ile Pro Lys Ala Arg Gln Pro Thr Gly Arg Ser Trp Gly Gln Pro Gly 65 70 75 80
- Tyr Pro Trp Pro Leu Tyr Ala Asn Glu Gly Leu Gly Trp Ala Gly Trp 85 90 95
- Leu Leu Ser Pro Arg Gly Ser Arg Pro Asn Trp Gly Pro Asn Asp Pro 100 105 110
- Arg Arg Lys Ser Arg Asn Leu Gly Lys Val Ile Asp Thr Leu Thr Cys 115 120 125
- Gly Phe Ala Asp Leu Met Gly Tyr Ile Pro Leu Val Gly Gly Pro Val 135 140
- Gly Gly Val Ala Arg Ala Leu Ala His Gly Val Arg Val Leu Glu Asp 145 150 155 160
- Gly Val Asn Tyr Pro Thr Gly Asn Leu Pro Gly Cys Ser Phe Ser Ile 165 170 175
- Phe Ile Leu Ala Leu Leu Ser Cys Leu Thr Val Pro Ala Ser Ala Val
- Pro Tyr Arg Asn Ala Ser Gly Ile Tyr His Val Thr Asn Asp Cys Pro 195 200 205
- Asn Ser Ser Ile Val Tyr Glu Ala Asp Asn Leu Ile Leu His Ala Pro 210 215 220
- Gly Cys Val Pro Cys Val Met Thr Gly Asn Val Ser Arg Cys Trp Val 225 230 235
- Gln Ile Thr Pro Thr Leu Ser Ala Pro Ser Leu Gly Ala Val Thr Ala 245 250 255
- Pro Leu Arg Arg Ala Val Asp Tyr Leu Ala Gly Gly Ala Ala Leu Cys 260 265 270
- Ser Ala Leu Tyr Val Gly Asp Ala Cys Gly Ala Leu Phe Leu Val Gly 275 280 285
- Gln Met Phe Thr Tyr Arg Pro Arg Gln His Ala Thr Val Gln Asn Cys 290 295 300
- Asn Cys Ser Ile Tyr Ser Gly His Val Thr Gly His Arg Met Ala 305 310 315

(2) INFORMATION FOR SEQ ID NO: 55:

(i) SEQUENCE CHARACTERISTICS:
(A) LENGTH: 354 base pairs
(B) TYPE: nucleic acid
(C) STRANDENNESS: single
(D) TOPOLOGY: linear

(ii) MOLECULE TYPE: CDNA

(iii) HYFOTHETICAL: NO

(iii) ANTI-SENSE: NO

(vii) IMMEDIATE SOURCE:
(B) CLONE: PC-1-37

(ix) FEATURE: (A) NAME/KEY: CDS (B) LOCATION: 1354	
(xi) SEQUENCE DESCRIPTION: SEQ ID NO: 55:	
ACCACCGGAG CTTCTATCAC ATACTCCACT TACGGCAAGT TCCTTGCTGA TGGAGGGTGT	60
TCAGGCGGCG CGCATGACGT GATCATATGC GACGAGTGCC ATTCCCAGGA CGCCACCACC	120
ATTCTTGGGA TAGGCACTGT CCTTGACCAG GCAGAGACGG CTGGAGCTAG GCTCGTCGTC	180
TTGGCCACGG NCACCCCTCC CGGCAGTGTG ACAACGCCCC ACCCCAACAT CGAGGAAGTG	240
GCCCTGCCTC AGGAGGGGGA GGTTCCCTTC TACGGCAGAG CCATTCCCCT TGCTTTTATA	300
ARGGGTGGTA GGCATCTCAT CTTCTGCCAT TCCAAGAAAA ATTGTGATGA ACTC	354
(2) INFORMATION FOR SEQ ID NO: 56: (i) SEQUENCE CHARACTERISTICS: (ii) LENGTH: 118 amino acids (ii) TYPE: amino acid (c) STRANDEDNESS: single (ii) TOPOLOGY: linear (ii) MOLECULE TYPE: protein	
(xi) SEQUENCE DESCRIPTION: SEQ ID NO: 56:	
Thr Thr Gly Ala Ser Ile Thr Tyr Ser Thr Tyr Gly Lys Phe Leu Ala 1 5 10 15	
Asp Gly Gly Cys Ser Gly Gly Ala His Asp Val Ile Ile Cys Asp Glu 20 25 30	

50 55 60	
Thr Pro Pro Gly Ser Val Thr Thr Pro His Pro Asn Ile Glu Glu 65 707075	Val 80
Ala Leu Pro Gln Glu Gly Glu Val Pro Phe Tyr Gly Arg Ala Ile $90 \ \ 95$	Pro
Leu Ala Phe Ile Lys Gly Gly Arg His Leu Ile Phe Cys His Ser $100 \hspace{1cm} 105 \hspace{1cm} 110 \hspace{1cm}$	Lys
Lys Asn Cys Asp Glu Leu 115	
(2) INFORMATION FOR SEQ ID NO: 57: (1) SEQUENCE CHARACTERISTICS: (A) LENGTH: 354 base pairs (B) TYPE: nucleic acid (C) STRANDENDESS: single (D) TOFOLOGY: linear (ii) MOLECULE TYPE: cDNA (iii) HYPOTHETICAL: NO (iii) ANTI-SENSE: NO (vii) IMMEDIATE SOURCE: (B) CLORE: PC-1-48 (ix) FEATURE: (A) NAME/KEY: CDS (B) LOCATION: 1354	
(xi) SEQUENCE DESCRIPTION: SEQ ID NO: 57:	
ACCACCGGAG CTTCTATCAC ATACTCCACT TACGGCAAGT TCCTTGCTGA TGGAGGGTGT	60
TCAGGCGGCG CGTATGACGT GATCATATGC GACGAGTGCC ATTCCCAGGA CGCCACCACC	120
ATTCTTGGGA TAGGCACTGT CCTTGACCAG GCAGAGACGG CTGGAGCTAG GCTCGTCGTC	180
TTGGNCACGG NCACCCCTCC CGGCAGTGTG ACAACGCCCC ACCCCAACAT CGAGGAAGTG	240
GCCCTGCCTC AGGAGGGGA GGTTCCCTTC TACGGNAGAG CCATTCCCCT TGCTTTTATA	. 300
AAGGGTGGTA GGCATCTCAT CTTCTGCCAT TCCAAGAAAA AATGTGATGA ACTT	354
(2) INFORMATION FOR SEQ ID NO: 58:	

(i) SEQUENCE CHARACTERISTICS:

- (A) LENGTH: 133 amino acids
- (B) TYPE: amino acid
- (C) STRANDEDNESS: single
- (D) TOPOLOGY: linear
- (ii) MOLECULE TYPE: protein
- (xi) SEQUENCE DESCRIPTION: SEO ID NO: 58:
- Thr Thr Gly Ala Ser Ile Thr Tyr Ser Thr Tyr Gly Lys Phe Leu Ala 1 5 10 15
- Asp Gly Gly Cys Ser Gly Gly Ala Tyr Asp Val Ile Ile Cys Asp Glu 20 25 30
- Cys His Ser Gln Asp Ala Thr Thr Ile Leu Gly Ile Gly Thr Val Leu 35 40 45
- Asp Gln Ala Glu Thr Ala Gly Ala Arg Leu Val Val Leu Xaa Thr Xaa 50 55 60
- Thr Pro Pro Gly Ser Val Thr Thr Pro His Pro Asn Ile Glu Glu Val 65 70 75 80
- Ala Leu Pro Gln Glu Gly Glu Val Pro Phe Tyr Xaa Arg Ala Ile Pro 85 90 95
- Leu Ala Phe Ile Lys Gly Gly Arg His Leu Ile Phe Cys His Ser Lys
 100 105 110

 Lys Lys Cys Asp Glu Leu Arg Gln Ala Thr Asp Gln Pro Gly Arg Glu
 115 120 125
- Arg Pro Trp Glu Tyr 130
- (2) INFORMATION FOR SEQ ID NO: 59:
 - (i) SEQUENCE CHARACTERISTICS:
 - (A) LENGTH: 357 base pairs
 - (B) TYPE: nucleic acid
 - (C) STRANDEDNESS: single
 (D) TOPOLOGY: linear
 - (ii) MOLECULE TYPE: cDNA
 - (iii) HYPOTHETICAL: NO
 - (iii) ANTI-SENSE: NO
 - (vii) IMMEDIATE SOURCE: (B) CLONE: PC-1-37
 - (ix) FEATURE:
 - (A) NAME/KEY: CDS

(B) LOCATION: 1..357

	DESCRIPTION:		

60	GGTGGGGGGC	CTTGGGTTCT	ATTACCANCA	CTTGGAGGTC	TGTCTCCGGA	ATGGCTTTCA
120	AGTCGGTAGG	CGGTAGCCAT	ACGGTGGGTT	CTACTGCTTG	CCCTGNCGNC	GTTGTGGCGA
180	CCAGCAATTT	AGGTATTATA	NCCGATAGGG	TGCCATCATT	CTGGGAAACC	ATCATCCTCT
240	TNCCATTGCC	ACGAAACACG	CCCTATATGG	GGCCTCGTTG	AGGAGTGCTC	GATGAGATGG
300	GGCTGAAACT	CCGGCCAGAA	ATCAGCACGA	GCTCGGCTTC	AAGAGAAAGT	GGACAATTCA
357	CACATAC	AGTTCTGGNC	AAGGCTGATC	TGTGTGGAAC	CAGCCACGTC	CTGAAGCCGG

(2) INFORMATION FOR SEQ ID NO: 60:

- (i) SEQUENCE CHARACTERISTICS:
 - (A) LENGTH: 128 amino acids
 - (B) TYPE: amino acid
 - (C) STRANDEDNESS: single
 (D) TOPOLOGY: linear
- (ii) MOLECULE TYPE: protein

(xi) SEQUENCE DESCRIPTION: SEQ ID NO: 60:

Met Ala Phe Met Ser Pro Asp Leu Glu Val Ile Thr Xaa Thr Trp Val 1 $$ 5

Leu Val Gly Gly Val Val Ala Thr Leu Xaa Xaa Tyr Cys Leu Thr Val 20 25 30

Gly Ser Val Ala Ile Val Gly Arg Ile Ile Leu Ser Gly Lys Pro Ala 35 40 45

Ile Ile Xaa Asp Arg Glu Val Leu Tyr Gln Gln Phe Asp Glu Met Glu 50 $\,$ 55 $\,$ 60 $\,$

Glu Cys Ser Ala Ser Leu Pro Tyr Met Asp Glu Thr Arg Xaa Ile Ala 65 707580

Gly Gln Phe Lys Glu Lys Val Leu Gly Phe Ile Ser Thr Thr Gly Gln 85 90 95

Lys Ala Glu Thr Leu Lys Pro Ala Ala Thr Ser Val Trp Asn Lys Ala 100 105 110

Asp Gln Phe Trp Xaa Thr Tyr Met Trp Asn Phe Ile Ser Gly Ile Gln
115 120 125

- (2) INFORMATION FOR SEQ ID NO: 61:
 - (i) SEQUENCE CHARACTERISTICS:

150	
(A) LENGTH: 357 base pairs (B) TYPE: nucleic acid (C) STRANDENESS: single (D) TOPOLOGY: linear	
(ii) MOLECULE TYPE: cDNA	
(iii) HYPOTHETICAL: NO	
(iii) ANTI-SENSE: NO	
(vii) IMMEDIATE SOURCE: (B) CLONE: PC-1-48	
(ix) FEATURE: (A) NAME/KEY: CDS (B) LOCATION: 1357	
(xi) SEQUENCE DESCRIPTION: SEQ ID NO: 61:	
ATGGCTTGCA TGTCTGCGGA CCTGGAGGTC ATTACCANCA CTTGGGTTCT GGTGGGGGGC	6
GTTGTGGCGN CCCTGGCGGC CTACTGCTTG ACGGTGGGTT CGGTAGCCAT AGTCGGTAGG	12
ATCATCCTCT CTGGGAAACC TGCCATCATT CCCGATAGGG AGGCATTATA CCANCAATTT	18
GATGAGATGG AGGAGTGCTC GGCCTCGTTG CCCTATATGG ACGAGACACG TGCCATTGCC	24
GGACAATTCA AAGAGAAAGT GCTCGGCTTC ATCAGCACGA CCGGCCAGAA GGCTGAAACT	30
CTGAAGCCGG CAGCCACGTC TGTGTGGAAC AAGGCTGANC AGTTCTGGGC CACATAC	35
(2) INFORMATION FOR SEQ ID NO: 62:	
(i) SEQUENCE CHARACTERISTICS: (A) LENGTH: 128 maino acids (B) TYPE: amino acid (C) STRANDEDNESS: single (D) TOPOLOGY: linear (ii) MOLECULE TYPE: protein	
(xi) SEQUENCE DESCRIPTION: SEQ ID NO: 62:	
Met Ala Cys Met Ser Ala Asp Leu Glu Val Ile Thr Xaa Thr Trp Val 1 510	
Leu Val Gly Val Val Ala Xaa Leu Ala Ala Tyr Cys Leu Thr Val 20 25 30	
Gly Ser Val Ala Ile Val Gly Arg Ile Ile Leu Ser Gly Lys Pro Ala 35 40	
Ile Ile Pro Asp Arg Glu Ala Leu Tyr Xaa Gln Phe Asp Glu Met Glu 50 55 60	

- Glu Cys Ser Ala Ser Leu Pro Tyr Met Asp Glu Thr Arg Ala Ile Ala 65 70 75 80
- Gly Gln Phe Lys Glu Lys Val Leu Gly Phe Ile Ser Thr Thr Gly Gln \$85\$ 90 95
- Lys Ala Glu Thr Leu Lys Pro Ala Ala Thr Ser Val Trp Asn Lys Ala 100 . 105 110

Xaa Gln Phe Trp Ala Thr Tyr Met Trp Asn Phe Ile Ser Gly Ile Gln
115 120 125

- (2) INFORMATION FOR SEQ ID NO: 63:
 - (i) SEQUENCE CHARACTERISTICS:
 - (A) LENGTH: 28 base pairs
 - (B) TYPE: nucleic acid
 - (C) STRANDEDNESS: single (D) TOPOLOGY: linear
 - (ii) MOLECULE TYPE: DNA (genomic)
 - (iii) HYPOTHETICAL: YES
 - (iii) ANTI-SENSE: NO
 - (ix) FEATURE:
 - (A) NAME/KEY: misc_feature
 - (B) LOCATION: 1.:28
 - (D) OTHER INFORMATION: /standard_name= "HCV Primer HCPr161"
 - (xi) SEQUENCE DESCRIPTION: SEO ID NO: 63:

ACCGGAGGCC AGGAGAGTGA TCTCCTCC

- (2) INFORMATION FOR SEQ ID NO: 64:
- (i) SEQUENCE CHARACTERISTICS:
 - (A) LENGTH: 28 base pairs
 - (B) TYPE: nucleic acid
 - (C) STRANDEDNESS: single
 - (D) TOPOLOGY: linear
 - (ii) MOLECULE TYPE: DNA (genomic)
 - (iii) HYPOTHETICAL: YES
 - (iii) ANTI-SENSE: YES
 - (ix) FEATURE:
 - (A) NAME/KEY: misc feature
 - (B) LOCATION: 1..28
 - (D) OTHER INFORMATION: /standard_name= "HCV Primer HCPr162"

(xi) SEQUENCE DESCRIPTION: SEQ ID NO: 64:		
GGGCTGCTCT ATCCTCATCG ACGCCATC		8
(2) INFORMATION FOR SEQ ID NO: 65:		
(i) SEQUENCE CHARACTERISTICS: (A) LENGTH: 28 base pairs (B) TYPE: nucleic acid (C) STRANDENIESS: single (D) TOPOLOGY: linear		
(ii) MOLECULE TYPE: DNA (genomic)		
(iii) HYPOTHETICAL: YES		
(iii) ANTI-SENSE: NO		
(ix) FEATURE: (A) NAME/KEY: misc_feature (B) LOCATION: 128 (D) OTHER INFORMATION: /standard_name= "FET163"	ICV Primer	
(xi) SEQUENCE DESCRIPTION: SEQ ID NO: 65:		
GCCAGAGGCT CGGAAGGCGA TCAGCGCT	2	8
(2) INFORMATION FOR SEQ ID NO: 66:		
(i) SEQUENCE CHARACTERISTICS: (A) LENOTH: 26 base pairs (B) TYPE: nucleic acid (C) STRANDENNESS: single (D) TOPOLOGY: linear		
(ii) MOLECULE TYPE: DNA (genomic)		
(iii) HYPOTHETICAL: YES		
(iii) ANTI-SENSE: YES		
(ix) FEATURE: (A) NAME/KEY: misc_feature (B) LOCATION: 128 (D) OTHER INFORMATION: /standard_name= "FHCP1164"	ICV Primer	
()) energy programmer and To Wo CC		

GAGCTGCTCT GTCCTCCTCG ACGCCGCA

(2) INFORMATION FOR SEQ ID NO: 67:

	(D) TOPOLOGY: linear	
(ii)	MOLECULE TYPE: DNA (genomic)	
(iii)	HYPOTHETICAL: YES	
(iii)	ANTI-SENSE: NO	
(ix)	FEATURE: (A) NAME/KEY: misc_feature (B) LOCATION: 128 (D) OTHER INFORMATION: /standard_name= "HCV Primer HCPr23"	
(xi)	SEQUENCE DESCRIPTION: SEQ ID NO: 67:	
CTCATGGG	GT ACATTCCGCT	20
(2) INFO	RMATION FOR SEQ ID NO: 68:	
(i)	SEQUENCE CHARACTERISTICS: (A) LENGTH: 27 base pairs (B) TYPE: nucleic acid (C) STRANDEDNESS: single (D) TOPOLOGY: linear	
(ii)	MOLECULE TYPE: DNA (genomic)	
(iii)	HYPOTHETICAL: YES	
(iii)	ANTI-SENSE: YES	
(ix)	FEATURE: (A) NAME/KEY: misc_feature (B) LOCATION: 128 (D) OTHER INFORMATION: /standard_name= "HCV Primer HCPr54"	
(xi)	SEQUENCE DESCRIPTION: SEQ ID NO: 68:	
CTATTACC	AG TTCATCATCA TATCCCA	27
(2) INFO	RMATION FOR SEQ ID NO: 69:	
(i)	SEQUENCE CHARACTERISTICS: (A) LENGTH: 24 base pairs (B) TYPE: nucleic acid (C) STRANDEDNESS: single (D) TOPOLOGY: linear	
(ii)	MOLECULE TYPE: DNA (genomic)	

(i) SEQUENCE CHARACTERISTICS:(A) LENGTH: 20 base pairs(B) TYPE: nucleic acid(C) STRANDEDNESS: single

- (iii) HYPOTHETICAL: YES
- (iii) ANTI-SENSE: NO
- (ix) FEATURE:
 - (A) NAME/KEY: misc_feature
 - (B) LOCATION: 1..28
 - (D) OTHER INFORMATION: /standard_name= "HCV Primer HCPr116"
- (xi) SEQUENCE DESCRIPTION: SEQ ID NO: 69:

TTTTAAATAC ATCATGRCTG YATG

(2) INFORMATION FOR SEQ ID NO: 70:

- - (i) SEQUENCE CHARACTERISTICS:
 - (A) LENGTH: 33 base pairs (B) TYPE: nucleic acid
 - (C) STRANDEDNESS: single
 - (D) TOPOLOGY: linear
 - (ii) MOLECULE TYPE: DNA (genomic)
 - (iii) HYPOTHETICAL: YES
 - (iii) ANTI-SENSE: YES
 - (ix) FEATURE:
 - (A) NAME/KEY: misc_feature
 - (B) LOCATION: 1..28
 - (D) OTHER INFORMATION: /standard_name= "HCV Primer HCPr66"
 - (xi) SEQUENCE DESCRIPTION: SEQ ID NO: 70:

CTATTATTGT ATCCCRCTGA TGAARTTCCA CAT

33

- (2) INFORMATION FOR SEQ ID NO: 71:
 - (i) SEQUENCE CHARACTERISTICS:
 - (A) LENGTH: 36 base pairs
 - (B) TYPE: nucleic acid
 - (C) STRANDEDNESS: single
 - (D) TOPOLOGY: linear
 - (ii) MOLECULE TYPE: DNA (genomic)
 - (iii) HYPOTHETICAL: YES
 - (iii) ANTI-SENSE: YES
 - (ix) FEATURE:
 - (A) NAME/KEY: misc feature

110 94/23001	155	1 C1/E1/4/01323
	(B) LOCATION: 128 (D) OTHER INFORMATION: /standard_name= "HCV Pri-HCFril8:	mer
(xi)	SEQUENCE DESCRIPTION: SEQ ID NO: 71:	
ACTAGTCG	AC TAYTGATCCR CTATRWARTT CCACAT	36
(2) INFO	RMATION FOR SEQ ID NO: 72:	
(i)	SEQUENCE CHRACTERISTICS: (A) LENGTH: 25 base pairs (B) TYPE: nucleic acid (C) STRANDEDNESS: single (D) TOPOLOGY: linear	
(ii)	MOLECULE TYPE: DNA (genomic)	
(iii)	HYPOTHETICAL: YES	
(iii)	ANTI-SENSE: NO	
	ZATURE: (A) NAMB/KEY: misc_feature (B) LOCATION: 128 (D) OTHER INFORMATION: /standard_name= "HCV Print HCPril7:	mer
	SEQUENCE DESCRIPTION: SEQ ID NO: 72:	
	AC ATCGCRCTGC ATGCA	25
	MATION FOR SEQ ID NO: 73: SEQUENCE CHARACTERISTICS: (A) LENGTH: 36 base pairs	
	(B) TYPE: nucleic acid (C) STRANDEDNESS: single (D) TOPOLOGY: linear	
(ii)	MOLECULE TYPE: DNA (genomic)	
(iii)	HYPOTHETICAL: YES	
(iii)	ANTI-SENSE: YES	
(ix) FF	EATURE: (A) NAME/KEY: misc_feature (B) LOCATION: 128 (D) OTHER INFORMATION: /standard_name= *HCV Print HCPr119:	mer

(2) INFORMATION FOR SEQ ID NO: 74:	
(i) SEQUENCE CHARACTERISTICS: (A) LENGTH: 34 base pairs (B) TYPE: nucleic acid (C) STRANDENNESS: Single (D) TOPOLOGY: linear	
(ii) MOLECULE TYPE: DNA (genomic)	
(iii) HYPOTHETICAL: YES	
(iii) ANTI-SENSE: NO	
(ix) FEATURE: (A) NAME/KEY: misc_feature (B) LOCATION: 128 (D) OTHER INFORMATION: /standard_name= "HCV Primer HCPri31:	
(xi) SEQUENCE DESCRIPTION: SEQ ID NO: 74:	
GGAATTCTAG ACCTCTGGGA YGARAYTGGA ARTG	34
(2) INFORMATION FOR SEQ ID NO: 75:	
(i) SEQUENCE CHARACTERISTICS: (A) LENGTH: 31 base pairs (B) TYPE: nucleic acid (C) STRANDEDNESS: single (D) TOPCLOGY: linear	
(ii) MOLECULE TYPE: DNA (genomic)	
(iii) HYPOTHETICAL: YES	
(iii) ANTI-SENSE: NO	
(ix) FEATURE: (A) NAME/KEY: misc_feature (B) LOCATION: 128 (D) OTHER INFORMATION: /standard_name= "HCV Primer HCPr130:	
(xi) SEQUENCE DESCRIPTION: SEQ ID NO: 75:	
GGAATTCTAG ACGCTAYCAR GCACGTTGYG C	31

(2) INFORMATION FOR SEQ ID NO: 76:

(i) SEQUENCE CHARACTERISTICS:

(A) LENGTH: 23 base pairs

(B) TYPE: nucleic acid

- (C) STRANDEDNESS: single
- (D) TOPOLOGY: linear
- (ii) MOLECULE TYPE: DNA (genomic)
- (iii) HYPOTHETICAL: YES
- (iii) ANTI-SENSE: NO
- (ix) FEATURE:
 - (A) NAME/KEY: misc feature
 - (B) LOCATION: 1..28
 - (D) OTHER INFORMATION: /standard_name= "HCV Primer HCPr134:
 - (xi) SEQUENCE DESCRIPTION: SEQ ID NO: 76:

CATATAGATG CCCACTTCCT ATC

23

- (2) INFORMATION FOR SEQ ID NO: 77:
 - (i) SEQUENCE CHARACTERISTICS:
 - (A) LENGTH: 16 base pairs
 - (B) TYPE: nucleic acid
 - (C) STRANDEDNESS: single
 - (D) TOPOLOGY: linear
 - (ii) MOLECULE TYPE: DNA (genomic)
 - (iii) HYPOTHETICAL: YES
 - (iii) ANTI-SENSE: YES
 - (ix) FEATURE:
 - (A) NAME/KEY: misc_feature
 - (B) LOCATION: 1..28
 - (D) OTHER INFORMATION: /standard_name= "HCV Primer HCPr3:
 - (xi) SEQUENCE DESCRIPTION: SEQ ID NO: 77:

GTGTGCCAGG ACCATC

- (2) INFORMATION FOR SEQ ID NO: 78:
 - (i) SEQUENCE CHARACTERISTICS:
 - (A) LENGTH: 20 base pairs (B) TYPE: nucleic acid
 - (C) STRANDEDNESS: single
 - (D) TOPOLOGY: linear
 - (ii) MOLECULE TYPE: DNA (genomic)

- (iii) HYPOTHETICAL: YES
- (iii) ANTI-SENSE: YES
- (ix) FEATURE:
 - (A) NAME/KEY: misc feature
 - (B) LOCATION: 1..28
 - (D) OTHER INFORMATION: /standard_name= "HCV Primer HCPr4:
- (xi) SEQUENCE DESCRIPTION: SEQ ID NO: 78:

GACATGCATG TCATGATGTA

20

- (2) INFORMATION FOR SEQ ID NO: 79:
 - (i) SEQUENCE CHARACTERISTICS:
 - (A) LENGTH: 29 base pairs (B) TYPE: nucleic acid
 - (C) STRANDEDNESS: single
 - (D) TOPOLOGY: linear
 - (ii) MOLECULE TYPE: DNA (genomic)
 - (iii) HYPOTHETICAL: NO
 - (iii) ANTI-SENSE: NO
 - (ix) FEATURE:
 - (A) NAME/KEY: misc feature
 - (B) LOCATION: 1..28
 - (D) OTHER INFORMATION: /standard_name= "HCV Primer HCPr152:
 - (xi) SEQUENCE DESCRIPTION: SEQ ID NO: 79:

TACGCCTCTT CTATATCGGT TGGGGCCTG

- (2) INFORMATION FOR SEQ ID NO: 80:
 - (i) SEQUENCE CHARACTERISTICS:
 - (A) LENGTH: 26 base pairs (B) TYPE: nucleic acid
 - (C) STRANDEDNESS: single
 - (D) TOPOLOGY: linear
 - (ii) MOLECULE TYPE: DNA (genomic)
 - (iii) HYPOTHETICAL: YES
 - (iii) ANTI-SENSE: NO

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- (ix) FEATURE:
 - (A) NAME/KEY: misc feature
 - (B) LOCATION: 1..28
 - (D) OTHER INFORMATION: /standard_name= "HCV Primer HCPr52:
- (xi) SEQUENCE DESCRIPTION: SEQ ID NO: 80:

ATGTTGGGTA AGGTCATCGA TACCCT

26

- (2) INFORMATION FOR SEQ ID NO: 81:
 - (i) SEQUENCE CHARACTERISTICS:
 - (A) LENGTH: 25 base pairs
 - (B) TYPE: nucleic acid
 - (C) STRANDEDNESS: single
 (D) TOPOLOGY: linear
 - (ii) MOLECULE TYPE: DNA (genomic)
 - -
 - (iii) HYPOTHETICAL: YES
 - (iii) ANTI-SENSE: NO
 - (ix) FEATURE:
 - (A) NAME/KEY: misc feature
 - (B) LOCATION: 1..28
 - (D) OTHER INFORMATION: /standard_name= "HCV Primer HCPr41:
 - (xi) SEQUENCE DESCRIPTION: SEQ ID NO: 81:

CCCGGGAGGT CTCGTAGACC GTGCA

- (2) INFORMATION FOR SEQ ID NO: 82:
 - (i) SEQUENCE CHARACTERISTICS:
 - (A) LENGTH: 29 base pairs
 - (B) TYPE: nucleic acid
 - (C) STRANDEDNESS: single
 (D) TOPOLOGY: linear
 - (ii) MOLECULE TYPE: DNA (genomic)
 - (iii) HYPOTHETICAL: YES
 - (iii) ANTI-SENSE: YES
 - (ix) FEATURE:
 - (A) NAME/KEY: misc feature
 - (B) LOCATION: 1..28
 - (D) OTHER INFORMATION: /standard_name= "HCV Primer HCPr40:

(xi) SEQUENCE DESCRIPTION: SEQ ID NO: 82:

CTATTAAAGA TAGAGAAAGA GCAACCGGG

- (2) INFORMATION FOR SEQ ID NO: 83:
 - (i) SEQUENCE CHARACTERISTICS:
 - (A) LENGTH: 12 amino acids
 - (B) TYPE: amino acid
 - (C) STRANDEDNESS: single
 - (D) TOPOLOGY: linear
 - (ii) MOLECULE TYPE: peptide
 - (iii) HYPOTHETICAL: NO
 - (viii) POSITION IN PROTEIN:
- (B) MAP POSITION: positions 192 to 203 of the V1 region of HCV type 3
 - (xi) SEQUENCE DESCRIPTION: SEQ ID NO: 83:
 - Leu Glu Trp Arg Asn Thr Ser Gly Leu Tyr Val Leu 1 5 10
- (2) INFORMATION FOR SEQ ID NO: 84:
 - (i) SEQUENCE CHARACTERISTICS:
 - (A) LENGTH: 12 amino acids
 - (B) TYPE: amino acid
 - (C) STRANDEDNESS: single (D) TOPOLOGY: linear
 - (ii) MOLECULE TYPE: peptide
 - (iii) HYPOTHETICAL: NO
- - (xi) SEQUENCE DESCRIPTION: SEQ ID NO: 84:
 - Val Pro Tyr Arg Asn Ala Ser Gly Ile Tyr His Val 1 $$ 5 $$ 10
- (2) INFORMATION FOR SEQ ID NO: 85:
 - (i) SEQUENCE CHARACTERISTICS:
 - (A) LENGTH: 11 amino acids
 - (B) TYPE: amino acid
 - (C) STRANDEDNESS: single

- (D) TOPOLOGY: linear
- (ii) MOLECULE TYPE: peptide
- (iii) HYPOTHETICAL: NO
- (viii) POSITION IN PROTEIN:

(B) MAP POSITION: positions 213 to 223 of the V2 region of HCV type 3 $\,$

(xi) SEQUENCE DESCRIPTION: SEQ ID NO: 85:

Val Tyr Glu Ala Asp Asp Val Ile Leu His Thr 1 5 10

- (2) INFORMATION FOR SEQ ID NO: 86:
 - (i) SEQUENCE CHARACTERISTICS:
 - (A) LENGTH: 11 amino acids
 - (B) TYPE: amino acid
 - (C) STRANDEDNESS: single (D) TOPOLOGY: linear
 - (ii) MOLECULE TYPE: peptide
 - (iii) HYPOTHETICAL: NO
 - (viii) POSITION IN PROTEIN:

(B) MAP POSITION: positions 213 to 233 of the V2 region of HCV $_{\cdot}$ type 5

(xi) SEQUENCE DESCRIPTION: SEQ ID NO: 86:

Val Tyr Glu Ala Asp Asn Leu Ile Leu His Ala 1 5 10

- (2) INFORMATION FOR SEQ ID NO: 87:
 - (i) SEQUENCE CHARACTERISTICS:
 - (A) LENGTH: 13 amino acids
 - (B) TYPE: amino acid
 - (C) STRANDEDNESS: single
 - (D) TOPOLOGY: linear
 - (ii) MOLECULE TYPE: peptide
 - (iii) HYPOTHETICAL: NO
- (viii) POSITION IN PROTEIN:
- (B) MAP POSITION: positions 230 to 242 of the V3 region of $\ensuremath{\text{HCV}}$ type 3

(xi) SEQUENCE DESCRIPTION: SEQ ID NO: 87:

Val Gln Asp Gly Asn Thr Ser Thr Cys Trp Thr Pro Val

- (2) INFORMATION FOR SEQ ID NO: 88:
 - (i) SEQUENCE CHARACTERISTICS:
 - (A) LENGTH: 13 amino acids
 - (B) TYPE: amino acid
 - (C) STRANDEDNESS: single (D) TOPOLOGY: linear
 - (ii) MOLECULE TYPE: peptide

 - (iii) HYPOTHETICAL: NO
- (viii) POSITION IN PROTEIN:

(B) MAP POSITION: positions 230 to 242 of the V3 region of HCV type 5 $\,$

(xi) SEQUENCE DESCRIPTION: SEQ ID NO: 88:

Val Met Thr Gly Asn Val Ser Arg Cys Trp Val Gln Ile 1 5 10

- (2) INFORMATION FOR SEQ ID NO: 89:
 - (i) SEQUENCE CHARACTERISTICS:
 - (A) LENGTH: 10 amino acids
 - (B) TYPE: amino acid
 - (C) STRANDEDNESS: single (D) TOPOLOGY: linear
 - (ii) MOLECULE TYPE: peptide
 - (iii) HYPOTHETICAL: NO
 - (viii) POSITION IN PROTEIN:

(B) MAP POSITION: positions 248 to 257 of the V4 region of HCV type 3 $\,$

(xi) SEQUENCE DESCRIPTION: SEQ ID NO: 89:

Val Arg Tyr Val Gly Ala Thr Thr Ala Ser

- (2) INFORMATION FOR SEQ ID NO: 90:
 - (i) SEQUENCE CHARACTERISTICS:
 - (A) LENGTH: 10 amino acids
 - (B) TYPE: amino acid
 - (C) STRANDEDNESS: single
 - (D) TOPOLOGY: linear

- (ii) MOLECULE TYPE: peptide
- (iii) HYPOTHETICAL: NO
- (viii) POSITION IN PROTEIN:

 (B) MAP POSITION: positions 248 to 257 of the V4 region of HCV type 5
 - (xi) SEQUENCE DESCRIPTION: SEQ ID NO: 90:
 - Ala Pro Ser Leu Gly Ala Val Thr Ala Pro
- (2) INFORMATION FOR SEQ ID NO: 91:
 - - (i) SEQUENCE CHARACTERISTICS:(A) LENGTH: 10 amino acids
 - (B) TYPE: amino acid
 - (C) STRANDEDNESS: single
 - (D) TOPOLOGY: linear
 - (ii) MOLECULE TYPE: peptide
 - (iii) HYPOTHETICAL: NO
- (xi) SEQUENCE DESCRIPTION: SEQ ID NO: 91:
 - Arg Pro Arg Arg His Gln Thr Val Gln Thr
 - 5 10
- (2) INFORMATION FOR SEQ ID NO: 92:
 - (i) SEQUENCE CHARACTERISTICS:
 - (A) LENGTH: 10 amino acids
 - (B) TYPE: amino acid
 - (C) STRANDEDNESS: single
 - (D) TOPOLOGY: linear
 - (ii) MOLECULE TYPE: peptide
 - (iii) HYPOTHETICAL: NO
- - (xi) SEQUENCE DESCRIPTION: SEQ ID NO: 92:

Arg Pro Arg Gln His Ala Thr Val Gln Asn 1 5 10

- (2) INFORMATION FOR SEQ ID NO: 93:
 - (i) SEQUENCE CHARACTERISTICS:
 - (A) LENGTH: 9 amino acids
 - (B) TYPE: amino acid
 - (C) STRANDEDNESS: single
 - (D) TOPOLOGY: linear
 - (ii) MOLECULE TYPE: peptide
 - (iii) HYPOTHETICAL: NO
 - (viii) POSITION IN PROTEIN:
 - (B) MAP POSITION: positions 70 to 78 of HCV type 5
 - (xi) SEQUENCE DESCRIPTION: SEO ID NO: 93:

Gln Pro Thr Gly Arg Ser Trp Gly Gln

- (2) INFORMATION FOR SEQ ID NO: 94:
 - (i) SEQUENCE CHARACTERISTICS:
 - (A) LENGTH: 8 amino acids
 - (B) TYPE: amino acid
 - (C) STRANDEDNESS: single (D) TOPOLOGY: linear
 - (ii) MOLECULE TYPE: peptide
 - (iii) HYPOTHETICAL: NO
 - (vi) ORIGINAL SOURCE:
 - (C) INDIVIDUAL ISOLATE: BR33 and BR36
 - (viii) POSITION IN PROTEIN:

(B) MAP POSITION: positions 230 to 237 of the V3 region of HCV type 3 $\,$

- (xi) SEQUENCE DESCRIPTION: SEO ID NO: 94:
- Val Gln Asp Gly Asn Thr Ser Thr
- (2) INFORMATION FOR SEQ ID NO: 95:
 - (i) SEQUENCE CHARACTERISTICS:
 - (A) LENGTH: B amino acids
 - (B) TYPE: amino acid
 - (C) STRANDEDNESS: single

- (D) TOPOLOGY: linear
- (ii) MOLECULE TYPE: peptide
- (iii) HYPOTHETICAL: NO
- (vi) ORIGINAL SOURCE:
 - (C) INDIVIDUAL ISOLATE: HD10
- (viii) POSITION IN PROTEIN:
- (B) MAP POSITION: positions 230 to 237 of the V3 region of HCV type 3
 - (xi) SEQUENCE DESCRIPTION: SEQ ID NO: 95:
 - Val Gln Asp Gly Asn Thr Ser Ala 1 5
- (2) INFORMATION FOR SEO ID NO: 96:
 - (i) SEQUENCE CHARACTERISTICS:
 - (A) LENGTH: 10 amino acids
 - (B) TYPE: amino acid
 - (C) STRANDEDNESS: single
 - (D) TOPOLOGY: linear
 - (ii) MOLECULE TYPE: peptide
 - (iii) HYPOTHETICAL: NO
 - (vi) ORIGINAL SOURCE:
 - (C) INDIVIDUAL ISOLATE: BR36
- (viii) POSITION IN PROTEIN:
- (B) MAP POSITION: positions 248 to 257 of the V4 region of HCV type 3 $\,$
 - (xi) SEQUENCE DESCRIPTION: SEQ ID NO: 96:
 - Val Lys Tyr Val Gly Ala Thr Thr Ala Ser 1 5 10
- (2) INFORMATION FOR SEO ID NO: 97:
 - (i) SEQUENCE CHARACTERISTICS:
 - (A) LENGTH: 20 amino acids
 - (B) TYPE: amino acid
 - (C) STRANDEDNESS: single
 - (D) TOPOLOGY: linear
 - (ii) MOLECULE TYPE: peptide
 - (iii) HYPOTHETICAL: NO
 - (vi) ORIGINAL SOURCE:
 - (C) INDIVIDUAL ISOLATE: BR36

(viii) POSITION IN GENOME:

(B) MAP POSITION: Positions 1688 to 1707 of HCV type 3

(xi) SEQUENCE DESCRIPTION: SEQ ID NO: 97:

Leu Gly Gly Lys Pro Ala Ile Val Pro Asp Lys Glu Val Leu Tyr Gln 1 5 10 15

Gln Tyr Asp Glu 20

- (2) INFORMATION FOR SEQ ID NO: 98:
 - (i) SEQUENCE CHARACTERISTICS:
 - (A) LENGTH: 20 amino acids
 - (B) TYPE: amino acid
 - (C) STRANDEDNESS: single
 - (D) TOPOLOGY: linear
 - (ii) MOLECULE TYPE: peptide
 - (iii) HYPOTHETICAL: NO
 - (vi) ORIGINAL SOURCE:
 (C) INDIVIDUAL ISOLATE: HD10
 - (viii) POSITION IN GENOME:
 - (B) MAP POSITION: positions 1688 to 1707 of HCV type 3
 - (xi) SEQUENCE DESCRIPTION: SEQ ID NO: 98:

Leu Gly Gly Lys Pro Ala Leu Val Pro Asp Lys Glu Val Leu Tyr Gln

1 10 15

Gln Tyr Asp Glu 20

- (2) INFORMATION FOR SEQ ID NO: 99:
 - (i) SEQUENCE CHARACTERISTICS:
 - (A) LENGTH: 20 amino acids
 - (B) TYPE: amino acid (C) STRANDEDNESS: single
 - (D) TOPOLOGY: linear
 - (ii) MOLECULE TYPE: peptide
 - (iii) HYPOTHETICAL: NO
 - (viii) POSITION IN GENOME:
 - (B) MAP POSITION: positions 1712 to 1731
 - (xi) SEQUENCE DESCRIPTION: SEO ID NO: 99:

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Ser Gln Ala Ala Pro Tyr Ile Glu Gln Ala Gln Val Ile Ala His Gln 1 5 10 15
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Phe Lys Glu Lys

- (2) INFORMATION FOR SEO ID NO: 100:
 - (i) SEQUENCE CHARACTERISTICS:
 - (A) LENGTH: 20 amino acids
 - (B) TYPE: amino acid
 - (C) STRANDEDNESS: single
 - (D) TOPOLOGY: linear
 - (ii) MOLECULE TYPE: peptide
 - (iii) HYPOTHETICAL: NO
 - (vi) ORIGINAL SOURCE:
 - (C) INDIVIDUAL ISOLATE: BR36
 - (viii) POSITION IN GENOME:
 - (B) MAP POSITION: positions 1724 to 1743 of HCV type 3
 - (xi) SEQUENCE DESCRIPTION: SEQ ID NO: 100:
 - Ile Ala His Gln Phe Lys Glu Lys Val Leu Gly Leu Leu Gln Arg Ala 1 $$ 5 $$ 10 $$ 15

Thr Gln Gln Gln

- (2) INFORMATION FOR SEO ID NO: 101:
 - (i) SEQUENCE CHARACTERISTICS:
 - (A) LENGTH: 20 amino acids
 - (B) TYPE: amino acid (C) STRANDEDNESS: single
 - (D) TOPOLOGY: linear
 - (ii) MOLECULE TYPE: peptide
 - (iii) HYPOTHETICAL: NO
 - (vi) ORIGINAL SOURCE:
 - (C) INDIVIDUAL ISOLATE: HD10
 - (viii) POSITION IN GENOME:
 - (B) MAP POSITION: positions 1724 to 1743 of HCV type 3
 - (xi) SEQUENCE DESCRIPTION: SEQ ID NO: 101:
 - Ile Ala His Gln Phe Lys Glu Lys Ile Leu Gly Leu Leu Gln Arg Ala 1 $$ 5 $$ 10 $$ 15

Thr Gln Gln Gln

- (2) INFORMATION FOR SEQ ID NO: 102:
 - (i) SEQUENCE CHARACTERISTICS:
 - (A) LENGTH: 20 amino acids
 - (B) TYPE: amino acid
 - (C) STRANDEDNESS: single
 - (D) TOPOLOGY: linear
 - (ii) MOLECULE TYPE: peptide
 - (iii) HYPOTHETICAL: NO
 - (viii) POSITION IN GENOME:
 - (B) MAP POSITION: positions 1688 to 1707 of HCV type 5
 - (xi) SEQUENCE DESCRIPTION: SEO ID NO: 102:
 - Leu Ser Gly Lys Pro Ala Ile Ile Pro Asp Arg Glu Ala Leu Tyr Gln 1 5 10 15
 - Gln Phe Asp Glu 20
- (2) INFORMATION FOR SEO ID NO: 103:
 - (i) SEQUENCE CHARACTERISTICS:
 - (A) LENGTH: 20 amino acids
 - (B) TYPE: amino acid
 - (C) STRANDEDNESS: single
 - (D) TOPOLOGY: linear
 - (ii) MOLECULE TYPE: peptide
 - (iii) HYPOTHETICAL: NO
 - (viii) POSITION IN GENOME:
 - (B) MAP POSITION: positions 1688 to 1707
 - (xi) SEQUENCE DESCRIPTION: SEQ ID NO: 103:
 - Leu Ser Gly Lys Pro Ala Ile Ile Pro Asp Arg Glu Val Leu Tyr Gln
 1 5 10 15
 - Gln Phe Asp Glu
 - 20
- (2) INFORMATION FOR SEQ ID NO: 104:
 - (i) SEQUENCE CHARACTERISTICS:
 - (A) LENGTH: 20 amino acids

- (B) TYPE: amino acid (C) STRANDEDNESS: single
- (D) TOPOLOGY: linear
- (D) TOPOLOGI: Tinear
- (ii) MOLECULE TYPE: peptide
- (iii) HYPOTHETICAL: NO
- (viii) POSITION IN GENOME:
 - (B) MAP POSITION: position 1712 to 1731 of HCV type 5
 - (xi) SEQUENCE DESCRIPTION: SEQ ID NO: 104:

Ser Ala Ser Leu Pro Tyr Met Asp Glu Thr Arg Ala Ile Ala Gly Gln 1 $$\rm 10^{\circ}$

Phe Lys Glu Lys

- (2) INFORMATION FOR SEO ID NO: 105:
 - (i) SEQUENCE CHARACTERISTICS:
 - (A) LENGTH: 20 amino acids
 - (B) TYPE: amino acid
 - (C) STRANDEDNESS: single
 (D) TOPOLOGY: linear
 - (ii) MOLECULE TYPE: peptide
 - (iii) HYPOTHETICAL: NO
 - (viii) POSITION IN GENOME:
 - (B) MAP POSITION: positions 1724 to 1743 of HCV type 5
 - (xi) SEQUENCE DESCRIPTION: SEQ ID NO: 105;

Ile Ala Gly Gln Phe Lys Glu Lys Val Leu Gly Phe Ile Ser Thr Thr

1 5 10 15

Gly Gln Lys Ala 20

- (2) INFORMATION FOR SEQ ID NO: 106:
 - (i) SEQUENCE CHARACTERISTICS:
 - (A) LENGTH: 340 base pairs (B) TYPE: nucleic acid
 - (B) IIFB, MICIEIC ACID
 - (C) STRANDEDNESS: single
 (D) TOPOLOGY: linear
 - (ii) MOLECULE TYPE: cDNA
 - (iii) HYPOTHETICAL: NO

ANTT-SENSE.	

(vii) IMMEDIATE SOURCE:
 (B) CLONE: GB48-3-10

(ix) FEATURE:

(A) NAME/KEY: CDS (B) LOCATION: 2..340

(xi) SEQUENCE DESCRIPTION: SEQ ID NO: 106:

C TCC ACT GTA ACC GAA AAG GAC ATC AGG GTC GAG GAG GAG GTC TAT

46

Ser Thr Val Thr 51u Lys Asp 1le Arg Val Glu Glu Val Tyr

1

10

CAG TOT TOT GAC CTG GAG CCC GAA GCC CGC AAG GCA ATT ACC GCC CTA 94 Gln Cys Cys Asp Leu Glu Pro Glu Ala Arg Lys Ala Ile Thr Ala Leu 20 25 30

ACA GAG AGA CTC TAC GTG GGC GGT CCC ATG CAT AAC AGC AAG GGA GAC
Thr Glu Arg Leu Tyr Val Gly Gly Pro Met His Asn Ser Lys Gly Asp
40
45

CTG TGC GGG TAT CGC AGA TGT CGC GCA AGC GGC GTC TAC ACC AGC AGC Leu Cys Gly Tyr Arg Arg Cys Arg Ala Ser Gly Val Tyr Thr Thr Ser 50 60 60

TTC GGG AAC ACA CTG ACG TGC TAC CTC AAA GCC TCA GCC GCT ATC AAA 238
Phe Gly Asn Thr Leu Thr Cys Tyr Leu Lys Ala Ser Ala Ala Ile Lys
65 70 75

GCG GCG GCG CTG AGA GAC TGC ACC ATG TTG GTC TGT GGT GAT GAC CTG 286 Ala Ala Gly Leu Arg Asp Cys Thr Met Leu Val Cys Gly Asp Asp Leu 80 85 90 95

GTT GTC ATC GCT GAG AGC GAT GGC GTA GAG GAG GAC AAA CGA CCC CTC 334 Val Val Ile Ala Glu Ser Asp Gly Val Glu Glu Asp Lys Arg Pro Leu 100 105

GGA GCC 340 Gly Ala

(2) INFORMATION FOR SEQ ID NO: 107:

(i) SEQUENCE CHARACTERISTICS:

(A) LENGTH: 113 amino acids

(B) TYPE: amino acid (D) TOPOLOGY: linear

(ii) MOLECULE TYPE: protein

(xi) SEQUENCE DESCRIPTION: SEQ ID NO: 107:

Ser Thr Val Thr Glu Lys Asp Ile Arg Val Glu Glu Val Tyr Gln 1 5 10 15

Cys Cys Asp Leu Glu Pro Glu Ala Arg Lys Ala Ile Thr Ala Leu Thr $20 \ 25 \ 30$

Glu Arg Leu Tyr Val Gly Gly Pro Met His Asn Ser Lys Gly Asp Leu 35 40 45

Cys Gly Tyr Arg Arg Cys Arg Ala Ser Gly Val Tyr Thr Thr Ser Phe 50 55 60

Gly Asn Thr Leu Thr Cys Tyr Leu Lys Ala Ser Ala Ala Ile Lys Ala 65 70 75 80

Ala Gly Leu Arg Asp Cys Thr Met Leu Val Cys Gly Asp Asp Leu Val 85 90 95

Val Ile Ala Glu Ser Asp Gly Val Glu Glu Asp Lys Arg Pro Leu Gly 100 105 110

Ala

- (2) INFORMATION FOR SEO ID NO: 108:
 - (i) SEQUENCE CHARACTERISTICS:
 - (A) LENGTH: 340 base pairs
 - (B) TYPE: nucleic acid (C) STRANDEDNESS: single
 - (D) TOPOLOGY: linear
 - (ii) MOLECULE TYPE: cDNA
 - (iii) HYPOTHETICAL: NO
 - (iii) ANTI-SENSE: NO
 - (vii) IMMEDIATE SOURCE: (B) CLONE: GB116-3-5
 - (ix) FEATURE:
 - (A) NAME/KEY: CDS
 - (B) LOCATION: 2..340
 - (xi) SEQUENCE DESCRIPTION: SEQ ID NO: 108:
- C TCC ACT GTA ACC GAA AAG GAC ATC AGG GTC GAG GAG GAG GTA TAT Ser Thr Val Thr Glu Lys Asp Ile Arg Val Glu Glu Val Tyr 1 5 10
- CAG TGT TGT GAC CTG GAG CCC GAG GCC CGC AGA GCA ATT ACC GCC CTA 94 Gln Cys Cys Asp Leu Glu Pro Glu Ala Arg Arg Ala Ile Thr Ala Leu
- ACA GAG AGA CTC TAC GTG GGC GGT CCC ATG CAT AAC AGC AGG GGA GAC
 Thr Glu Arg Leu Tyr Val Gly Gly Pro Met His Asn Ser Arg Gly Asp
 40
 45

(D) TOPOLOGY: linear

(ii) MOLECULE TYPE: protein

(xi) SEQUENCE DESCRIPTION: SEQ ID NO: 109:

Ser Thr Val Thr Glu Lys Asp Ile Arg Val Glu Glu Glu Val Tyr Gln
1 10 15

Cys Cys Asp Leu Glu Pro Glu Ala Arg Arg Ala Ile Thr Ala Leu Thr
20 25 30

Glu Arg Leu Tyr Val Gly Gly Pro Met His Asn Ser Arg Gly Asp Leu
35 45

Cys Gly Tyr Arg Arg Cys Arg Ala Ser Gly Val Tyr Thr Thr Ser Phe
50 55 60

Gly Asn Thr Leu Thr Cys Tyr Leu Lys Ala Ser Ala Ala Ile Arg Ala
65 70 70

Ala Gly Leu Arg Asp Cys Thr Met Leu Val Cys Gly Asp Asp Leu Val
95

Val Ile Ala Glu Ser Asp Gly Val Glu Glu Asp Lys Arg Ala Leu Gly
100 105 110

(2) INFORMATION FOR SEO ID NO: 110:

(i) SEQUENCE CHARACTERISTICS:

		(B) T C) S	YPE: TRAN OPOL	nuc DEDN	leic ESS:	aci sin	d	s								
	(ii) MO	LECU	LE T	YPE:	cDN	Ά										
	(iii) ну	ротн	ETIC	AL:	NO											
	(111) AN	TI-S	ENSE	: NO												
	(vii			ATE LONE			3-8										
	(ix	(.		E: AME/ OCAT			340										
	(xi)	SE	QUEN	CE D	ESCR:	IPTI	: MC	SEQ	ID N): 1	10:						
				CC G					rg Va					al T		4	6
CAG Gln	TGT Cys	TGT Cys	GAC Asp	CTG Leu 20	GAG Glu	CCC Pro	GAA Glu	GCC Ala	CGC Arg 25	AAG Lys	GTA Val	ATT Ile	ACC Thr	GCC Ala 30	CTA Leu	9-	4
															GAC Asp	14:	2
				cgc Arg											AGC Ser	190	O
				CTG Leu											AGG Arg	231	3
				AGA Arg												286	5
				GAG Glu 100												334	ì
GA Bly	GTC Val															340)

- (i) SEQUENCE CHARACTERISTICS:
 - (A) LENGTH: 113 amino acids
 (B) TYPE: amino acid
 - (D) TOPOLOGY: linear
- (ii) MOLECULE TYPE: protein
- (xi) SEQUENCE DESCRIPTION: SEQ ID NO: 111:

Ser Thr Val Thr Glu Lys Asp Ile Arg Val Glu Glu Glu Val Tyr Gln 1 $$ 15

Cys Cys Asp Leu Glu Pro Glu Ala Arg Lys Val Ile Thr Ala Leu Thr 20 25 30

Glu Arg Leu Tyr Val Gly Gly Pro Met His Asn Ser Lys Gly Asp Leu 35 40 45

Cys Gly Tyr Arg Arg Cys Arg Ala Ser Gly Val Tyr Thr Thr Ser Phe 50 60

Gly Asn Thr Leu Thr Cys Tyr Leu Lys Ala Ser Ala Ala Ile Arg Ala 65 70 75 80

Ser Gly Leu Arg Asp Cys Thr Met Leu Val Tyr Gly Asp Asp Leu Val 85 90 95

Val Ile Ala Glu Ser Asp Gly Val Glu Glu Asp Lys Arg Ala Leu Gly

Val

- (2) INFORMATION FOR SEO ID NO: 112:
 - (i) SEQUENCE CHARACTERISTICS:
 - (A) LENGTH: 340 base pairs
 - (B) TYPE: nucleic acid
 - (C) STRANDEDNESS: single
 (D) TOPOLOGY: linear
 - (ii) MOLECULE TYPE: cDNA
 - (iii) HYPOTHETICAL: NO
 - (iii) ANTI-SENSE: NO
 - (vii) IMMEDIATE SOURCE:
 (B) CLONE: GB358-3-3
 - (ix) FEATURE:
 - (A) NAME/KEY: CDS
 - (B) LOCATION: 2..340
 - (xi) SEQUENCE DESCRIPTION: SEQ ID NO: 112:
- C TCC ACT GTA ACC GAA AAG GAC ATC AGG GTC GAG GAG GAG GTG TAT

	S	er T	hr V	al T	hr G	lu L 5	ys A	sp I	le A	al G 10	lu G	lu G	lu V	yr 15	
			TGT Cys											CTA Leu	. 94
			AGA Arg												142
			GGG Gly 50												190
			AAC Asn												238
			GGG Gly												286
			ATC Ile												334
C	IGA	GCC													340

(2) INFORMATION FOR SEQ ID NO: 113:

Gly Ala

- (i) SEQUENCE CHARACTERISTICS:
 - (A) LENGTH: 113 amino acids
 - (B) TYPE: amino acid (D) TOPOLOGY: linear
- (ii) MOLECULE TYPE: protein
- (xi) SEQUENCE DESCRIPTION: SEQ ID NO: 113:

Ser Thr Val Thr Glu Lys Asp Ile Arg Val Glu Glu Glu Val Tyr Gln

Cys Cys Asp Leu Glu Pro Glu Ala Arg Lys Ala Ile Thr Ala Leu Thr \$20\$

Glu Arg Leu Tyr Val Gly Gly Pro Met His Asn Ser Lys Gly Asp Leu 35 40 45

Cys Gly Tyr Arg Arg Cys Arg Ala Ser Gly Val Tyr Thr Thr Ser Phe 50 60

Gly Asn Thr Leu Thr Cys Tyr Leu Lys Ala Ser Ala Ala Ile Arg Ala 65 75 80

Ala Gly Leu Arg Asp Cys Thr Met Leu Val Cys Gly Asp Asp Leu Val 85 90

Val Ile Ala Glu Ser Asp Gly Val Glu Glu Asp Lys Arg Ala Leu Gly 100 105 110

Ala

121	THEORMATION	FOD	CEO	TD	NTO .	114

(i) SEQUENCE CHARACTERISTICS:

- (A) LENGTH: 340 base pairs
- (B) TYPE: nucleic acid
- (C) STRANDEDNESS: single
- (D) TOPOLOGY: linear
- (ii) MOLECULE TYPE: cDNA
- (iii) HYPOTHETICAL: NO
- (iii) ANTI-SENSE: NO
- (vii) IMMEDIATE SOURCE:
 (B) CLONE: GB549-3-6
- (ix) FEATURE:
 - (A) NAME/KEY: CDS
 - (B) LOCATION: 2..340

(xi) SEQUENCE DESCRIPTION: SEQ ID NO: 114:

C	TCC	ACG	GTG	ACC	GAA	AGG	GAT	ATC	AGG	ACC	GAG	GAA	GAG	ATC	TAC	46
	Ser	Thr	Val	Thr	Glu	Arg	Asp	Ile	Arg	Thr	Glu	Glu	Glu	Ile	Tyr	
	1				5					10					15	

- ACG GAA AGA CTC TAC GTG GGC GGT CCC ATG TAC AAC TCC AAG GGG GAC
 Thr Glu Arg Leu Tyr Val Gly Gly Pro Met Tyr Asn Ser Lys Gly Asp
 35
 40
 45
- CTA TGC GGG CAA CGG AGG TGC CGC GCA AGC GGG GTC TAC ACC ACC AGC Leu Cys Gly Gln Arg Arg Cys Arg Ala Ser Gly Val Tyr Thr Thr Ser 50 55 60
- TTC GGG AAC ACT GTA ACG TGT TAT CTC AAG GCC GTT GCG GCT ACT AGG 238
 Phe Gly Asn Thr Val Thr Cys Tyr Leu Lys Ala Val Ala Ala Thr Arg
 55 70 75
- GCC GCA GGT CTG AAA GGT TGC AGC ATG CTG GTT TGT GGA GAC GAC TTA
 Ala Ala Gly Leu Lys Gly Cys Ser Met Leu Val Cys Gly Asp Asp Leu
 80 85 90 95

GTC GTC ATC TGC GAG AGC GGC GGC GTA GAG GAG GAT GCA AGA GAC CTC Val Val Ile Cys Glu Ser Gly Gly Val Glu Glu Asp Ala Arg Ala Leu 100 105 110

CGA GCC Arg Ala 340

334

- (2) INFORMATION FOR SEQ ID NO: 115:
 - (i) SEQUENCE CHARACTERISTICS:
 - (A) LENGTH: 113 amino acids
 - (B) TYPE: amino acid (D) TOPOLOGY: linear
 - .., ------
 - (ii) MOLECULE TYPE: protein
 - (xi) SEQUENCE DESCRIPTION: SEQ ID NO: 115:

Ser Thr Val Thr Glu Arg Asp Ile Arg Thr Glu Glu Glu Ile Tyr Glu 1 5 10 15

Cys Cys Asp Leu Glu Pro Glu Ala Arg Lys Val Ile Ser Ala Leu Thr \$20\$ \$30\$

Glu Arg Leu Tyr Val Gly Gly Pro Met Tyr Asn Ser Lys Gly Asp Leu 35 40 45

Gly Asn Thr Val Thr Cys Tyr Leu Lys Ala Val Ala Ala Thr Arg Ala 65 70 75 80

Ala Gly Leu Lys Gly Cys Ser Met Leu Val Cys Gly Asp Asp Leu Val 85 90 95

Val Ile Cys Glu Ser Gly Gly Val Glu Glu Asp Ala Arg Ala Leu Arg 100 105 110

Ala

- (2) INFORMATION FOR SEQ ID NO: 116:
 - (i) SEQUENCE CHARACTERISTICS:
 - (A) LENGTH: 340 base pairs
 - (B) TYPE: nucleic acid
 - (C) STRANDEDNESS: single
 (D) TOPOLOGY: linear
 - (ii) MOLECULE TYPE: cDNA
 - .__, ..._
 - (iii) HYPOTHETICAL: NO
 - (iii) ANTI-SENSE: NO

(vii) IMMEDIATE SOURCE:

(B) CLONE: GB809-3-1													
(ix) FEATURE: (A) NAME/KEY: CDS (B) LOCATION: 2340													
· · · · ·													
(xi) SEQUENCE DESCRIPTION: SEQ ID NO: 116:													
C TCC ACT GTG ACT GAG AGA GAC ATC AAG GTC GAA GAA GAA GTC TAT	46												
Ser Thr Val Thr Glu Arg Asp Ile Lys Val Glu Glu Glu Val Tyr													
CAG TGT TGT GAT CTG GAG CCC GAG GCC CGC AAG GTA ATA GCC GCC CTC	94												
Gln Cys Cys Asp Leu Glu Pro Glu Ala Arg Lys Val Ile Ala Ala Leu													
20 25 30													
ACG GAG AGA CTC TAC GTG GGC GGC CCC ATG CAT AAC AGC AAG GGA GAC	142												
Thr Glu Arg Leu Tyr Val Gly Gly Pro Met His Asn Ser Lys Gly Asp 35 40 45													
35 40 45													
CTT TGC GGG TAT CGT AGA TGC CGC GCG AGC GGC GTA TAC ACC ACC AGC	190												
Leu Cys Gly Tyr Arg Arg Cys Arg Ala Ser Gly Val Tyr Thr Thr Ser													
•													
TTC GGG AAC ACA ATG ACG TGC TAC CTT AAG GCC TCA GCA GCC ATC AGG	238												
Phe Gly Asn Thr Met Thr Cys Tyr Leu Lys Ala Ser Ala Ala Ile Arg 65 70 75													
GCT GCG GGG CTA AAG GAT TGC ACC ATG CTG GTT TGC GGT GAC GAC CTA	286												
Ala Ala Gly Leu Lys Asp Cys Thr Met Leu Val Cys Gly Asp Asp Leu 80 85 90 95.													
GTC GTG ATC GCC GAG AGC GGT GGC GTT GAG GAG GAC AAA CGA GCC CTC Val Val Ile Ala Glu Ser Gly Gly Val Glu Glu Asp Lys Arg Ala Leu	334												
100 105 110													
GGA GCT Gly Ala	340												
THE STATE OF													

- (2) INFORMATION FOR SEQ ID NO: 117:
 - (i) SEQUENCE CHARACTERISTICS:(A) LENGTH: 113 amino acids
 - (B) TYPE: amino acid
 - (D) TOPOLOGY: linear
 - (ii) MOLECULE TYPE: protein
 - (xi) SEQUENCE DESCRIPTION: SEQ ID NO: 117:
- Ser Thr Val Thr Glu Arg Asp Ile Lys Val Glu Glu Glu Val Tyr Gln 1 5 10 15

Cys	Cys	Asp	Leu	Glu	Pro	Glu	Ala	Arg	Lys	Val	Ile	Ala	Ala	Leu	Thr
			20					25					30		

Glu Arg Leu Tyr Val Gly Gly Pro Met His Asn Ser Lys Gly Asp Leu 35 40 45

Cys Gly Tyr Arg Arg Cys Arg Ala Ser Gly Val Tyr Thr Thr Ser Phe 50 55 60

Gly Asn Thr Met Thr Cys Tyr Leu Lys Ala Ser Ala Ala Ile Arg Ala 65 $^{\circ}$ 70 $^{\circ}$ 75

Ala Gly Leu Lys Asp Cys Thr Met Leu Val Cys Gly Asp Asp Leu Val 85 90 95

Val Ile Ala Glu Ser Gly Gly Val Glu Glu Asp Lys Arg Ala Leu Gly 100 105 110

Ala

- (2) INFORMATION FOR SEQ ID NO: 118:
 - (i) SEQUENCE CHARACTERISTICS:
 - (A) LENGTH: 574 base pairs
 - (B) TYPE: nucleic acid (C) STRANDEDNESS: single
 - (D) TOPOLOGY: linear
 - (ii) MOLECULE TYPE: cDNA
 - (iii) HYPOTHETICAL: NO
 - (iii) ANTI-SENSE: NO
 - (vii) IMMEDIATE SOURCE: (B) CLONE: GB358-4-1
 - (ix) FEATURE:
 - (A) NAME/KEY: CDS
 - (B) LOCATION: 1..574
 - (xi) SEQUENCE DESCRIPTION: SEQ ID NO: 118:

ACT TGC GGC TTT GCC GAC CTC ATG GGA TAC ATC CCG CTC GTA GGC GCC
Thr Cys Gly Phe Ala Asp Leu Met Gly Tyr Ile Pro Leu Val Gly Ala
1 5 10 15

CCT GTG GGT GGC GTC GCC AGG GCC CTG GCA CAC GGT GTT AGG GCT GTG
Pro Val Gly Gly Val Ala Arg Ala Leu Ala His Gly Val Arg Ala Val
20
25
30

GAG GAC GGG ATC AAT TAT GCG ACA GGG AAT CTT CCC GGT TGC TCT TTC
Glu Asp Gly Ile Asn Tyr Ala Thr Gly Asn Leu Pro Gly Cys Ser Phe
35
40

(2) INFORMATION FOR SEQ ID NO: 119:

- (i) SEQUENCE CHARACTERISTICS:
 - (A) LENGTH: 191 amino acids
 - (B) TYPE: amino acid
- (D) TOPOLOGY: linear
- (ii) MOLECULE TYPE: protein
- (xi) SEQUENCE DESCRIPTION: SEQ ID NO: 119:

Thr Cys Gly Phe Ala Asp Leu Met Gly Tyr Ile Pro Leu Val Gly Ala 1 $$ 10 $$ 15

Pro Val Gly Gly Val Ala Arg Ala Leu Ala His Gly Val Arg Ala Val

Glu Asp Gly Ile Asn Tyr Ala Thr Gly Asn Leu Pro Gly Cys Ser Phe

Ser Ile Phe Leu Leu Ala Leu Leu Ser Cys Leu Thr Val Pro Thr Ser

50

Ala Val Asn Tyr Arg Asn Ala Ser Gly Ile Tyr His Ile Thr Asn Asp 70

Cys Pro Asn Ser Ser Ile Val Tyr Glu Thr Glu His His Ile Leu His 85 90

Leu Pro Gly Cys Leu Pro Cys Val Arg Val Gly Asn Gln Ser Arg Cys

Trp Val Ala Leu Thr Pro Thr Val Ala Ala Pro Tyr Ile Gly Ala Pro

Leu Glu Ser Leu Arg Ser His Val Asp Leu Met Val Gly Ala Ala Thr 135

Ala Cys Ser Ala Leu Tyr Ile Gly Asp Leu Cys Gly Gly Val Phe Leu

Val Gly Gln Met Phe Ser Phe Gln Pro Arg Arg His Trp Thr Thr Gln 165

Asp Cys Asn Cys Ser Ile Tyr Ala Gly His Val Thr Gly His Arg

- (2) INFORMATION FOR SEO ID NO: 120:
 - (i) SEQUENCE CHARACTERISTICS:
 - (A) LENGTH: 574 base pairs
 - (B) TYPE: nucleic acid
 - (C) STRANDEDNESS: single (D) TOPOLOGY: linear
 - (ii) MOLECULE TYPE: cDNA
 - (iii) HYPOTHETICAL: NO
 - (iii) ANTI-SENSE: NO
 - (vii) IMMEDIATE SOURCE:
 - (B) CLONE: GB549-4-3
 - (ix) FEATURE:
 - (A) NAME/KEY: CDS
 - (B) LOCATION: 1..574
 - (xi) SEQUENCE DESCRIPTION: SEQ ID NO: 120:

ACG TGC GGC TTT GCC GAC CTC ATG GGA TAC ATC CCG CTC GTG GGC GCC Thr Cys Gly Phe Ala Asp Leu Met Gly Tyr Ile Pro Leu Val Gly Ala

CCT GTG GGT GGC GTC GCC AGG GCC TTG GCA CAT GGT GTC AGG GCC GTG Pro Val Gly Gly Val Ala Arg Ala Leu Ala His Gly Val Arg Ala Val 20 25

96

48

GAG	GAC	GGG	ATT	AAC	тат	GCA	ACA	caa	ייי א א	CTTT.	ccc	com	mca	maa	mmm	
			Ile													144
oru		35			-7-	ALU	40	GLY	Aon	пец	FLO	45	Cys	ser	Pile	
TCT	ATC	TTC	CTT	CTA	GCA	CTT		TCG	TGC	TTG	ACT		ccc	GCC	TCG	192
			Leu													132
	50					55			-2-		60			,,,,,	DCI	
GCG	CAG	CAC	TAC	CGG	AAC	ATC	TCG	GGC	ATT	TAT	CAC	GTC	ACC	ддт	GAC	240
			Tyr													240
65					70					75			****	*****	80	
															00	
TGC	CCG	AAC	TCT	AGT	ATA	GTG	TAT	GAA	GCT	GAC	CAT	CAT	ATC	ATG	CAT	288
Cys	Pro	Asn	Ser	Ser	Ile	Val	Tyr	Glu	Ala	Asp	His	His	Ile	Met	His	
				85					90					95		
			TGT													336
Leu	Pro	Gly	Cys	Val	Pro	Cys	Val		Thr	Gly	Asn	Thr	Ser	Arg	Cys	
			100					105					110			
			TTA													384
Trp	Val		Leu	Thr	Pro	Thr		Ala	Ala	Pro	Tyr		Gly	Ala	Pro	
		115					120					125				
oma.	C22	maa	ATG	000	000	~~~	ama	~~~	mma							
			Met													432
Deu	130	per	Mec	Arg	ALG	135	vai	мвр	Leu	met	140	GIY	Ата	ALA	Thr	
	130					133					140					
GTC	TGC	TCG	GCC	CTG	TAC	ATC	GGA	GAC	CTT	TGC	ADD	GGT	GTC	TTC	CTG	480
			Ala													-00
145	-				150					155	2	2			160	
GTC	GGG	CAG	ATG	TTC	ACC	TTC	CGG	CCG	CGC	CGC	CAT	TGG	ACT	ACC	CAG	528
Val	Gly	Gln	Met	Phe	Thr	Phe	Arg	Pro	Arg	Arg	His	Trp	Thr	Thr	Gln	
				165					170					175		
			TGC												A	574
Asp	Cys	Asn	Cys	Ser	Ile	Tyr	Asp		His	Ile	Thr	Gly		Arg		
			180					185					190			

- (2) INFORMATION FOR SEQ ID NO: 121:
 - (i) SEQUENCE CHARACTERISTICS:
 - (A) LENGTH: 191 amino acids
 - (B) TYPE: amino acid
 - (D) TOPOLOGY: linear
 - (ii) MOLECULE TYPE: protein
 - (xi) SEQUENCE DESCRIPTION: SEQ ID NO: 121:

Thr Cys Gly Phe Ala Asp Leu Met Gly Tyr Ile Pro Leu Val Gly Ala 1 10 15

Pro Val Gly Val Ala Arg Ala Leu Ala His Gly Val Arg Ala Val 20 25 30 Glu Asp Gly Ile Asn Tyr Ala Thr Gly Asn Leu Pro Gly Cys Ser Phe 35 40 45

Ser Ile Phe Leu Leu Ala Leu Leu Ser Cys Leu Thr Val Pro Ala Ser

Ala Gln His Tyr Arg Asn Ile Ser Gly Ile Tyr His Val Thr Asn Asp 65 70 75 80

Cys Pro Asn Ser Ser Ile Val Tyr Glu Ala Asp His His Ile Met His 85 90 95

Leu Pro Gly Cys Val Pro Cys Val Arg Thr Gly Asn Thr Ser Arg Cys 100 105 110

Trp Val Pro Leu Thr Pro Thr Val Ala Ala Pro Tyr Val Gly Ala Pro 115 120 125

Leu Glu Ser Met Arg Arg His Val Asp Leu Met Val Gly Ala Ala Thr 130 135 140

Val Cys Ser Ala Leu Tyr Ile Gly Asp Leu Cys Gly Gly Val Phe Leu 145 150 155 160

Val Gly Gln Met Phe Thr Phe Arg Pro Arg Arg His Trp Thr Thr Gln 165 170 175

Asp Cys Asn Cys Ser Ile Tyr Asp Gly His Ile Thr Gly His Arg 180 185 190

- (2) INFORMATION FOR SEQ ID NO: 122:
 - (i) SEQUENCE CHARACTERISTICS:
 - (A) LENGTH: 574 base pairs
 - (B) TYPE: nucleic acid
 - (C) STRANDEDNESS: single (D) TOPOLOGY: linear
 - (ii) MOLECULE TYPE: cDNA
 - (au) (10mmoumb 111m) Obia
 - (iii) HYPOTHETICAL: NO
 - (iii) ANTI-SENSE: NO
 - (vii) IMMEDIATE SOURCE:
 - (B) CLONE: GB809-4-3
 - (ix) FEATURE:
 - (A) NAME/KEY: CDS
 - (B) LOCATION: 1..574
 - (xi) SEQUENCE DESCRIPTION: SEQ ID NO: 122:

ACG TGC GGC TTC GCC GAC CTC ATG GGA TAC ATC CCG CTC GTG GGC GCC

								10	4							
Thr 1	Cys	Gly	Phe	Ala 5	Asp	Leu	Met	Gly	Tyr 10	Ile	Pro	Leu	Val	Gly 15	Ala	
CCC	GTT	GGG	GGC	GTC	GCC	AGG	GCC	CTG	GCG	CAT	GGC	GTC	AGG	GCT	GTG	96
Pro	Val	Gly	Gly 20	Val	Ala	Arg	Ala	Leu 25	Ala	His	Gly	Val	Arg 30	Ala	Val	
			ATT													144
Glu	Asp	Gly 35	Ile	Asn	Tyr	Ala	Thr 40	Gly	Asn	Leu	Pro	Gly 45	Сув	Ser	Phe	
															TCA	192
Ser	Ile 50	Phe	Leu	Leu	Ala	Leu 55	Leu	Ser	Cys	Leu	Thr 60	Val	Pro	Ala	Ser	
			TAC													240
Ala 65	Glu	His	Tyr	Arg	Asn 70	Ala	Ser	Gly	Ile	Tyr 75	His	Ile	Thr	Asn	Asp 80	
TGT	CCG	AAT	TCC	AGC	GTA	GTC	TAT	GAA	ACT	GAC	CAC	CAT	ATA	TTG	CAC	288
Cys	Pro	Asn	Ser	Ser 85	Val	Val	Tyr	Glu	Thr 90	Asp	His	His	Ile	Leu 95	His	
TTG	CCG	GGG	TGC	GTA	ccc	TGC	GTG	AGG	GCC	GGG	AAC	GTG	TCT	CGT	TGC	336
			Cys 100													
			GTA													384
Trp	Thr	Pro 115	Val	Thr	Pro	Thr	120	Ala	Ala	Val	ser	Met 125	Asp	Ala	Pro	
			TTC													432
Leu	Glu 130	Ser	Phe	Arg	Arg	His 135	Val	Asp	Leu	Met	Val 140	Gly	Ala	Ala	Thr	
			GTC													480
	Cys	Ser	Val	Leu		Val	Gly	Asp	Leu		Gly	Gly	Ala	Phe		
145					150					155					160	
GTG	GGG	CAG	ATG	TTC	ACC	TTC	CAG	CCG	CGT	CGC	CAC	TGG	ACC	ACG	CAG	528
Val	Gly	Gln	Met	Phe 165	Thr	Phe	Gln	Pro	Arg 170	Arg	His	Trp	Thr	Thr 175	Gln	
GAT	TGT	AAT	TGC	TCC	ATC	TAT	ACT	GGC	CAT	ATC	ACC	GGC	CAC	AGG	A	574
Asp	Cys	Asn	Cys 180	Ser				Gly 185					His 190	Arg		

- (2) INFORMATION FOR SEQ ID NO: 123:
 - (i) SEQUENCE CHARACTERISTICS:
 - (A) LENGTH: 191 amino acids
 - (B) TYPE: amino acid
 - (D) TOPOLOGY: linear
 - (ii) MOLECULE TYPE: protein
 - (xi) SEQUENCE DESCRIPTION: SEQ ID NO: 123:

Thr Cys Gly Phe Ala Asp Leu Met Gly Tŷr Ile Pro Leu Val Gly Ala 1 5 10 15

Pro Val Gly Val Ala Arg Ala Leu Ala His Gly Val Arg Ala Val 20 25 30

Glu Asp Gly Ile Asn Tyr Ala Thr Gly Asn Leu Pro Gly Cys Ser Phe $35 \hspace{1cm} 40 \hspace{1cm} 45$

Ser Ile Phe Leu Leu Ala Leu Leu Ser Cys Leu Thr Val Pro Ala Ser 50 55

Ala Glu His Tyr Arg Asn Ala Ser Gly Ile Tyr His Ile Thr Asn Asp 65 70 75 80

Cys Pro Asn Ser Ser Val Val Tyr Glu Thr Asp His His Ile Leu His 85 90 95

Leu Pro Gly Cys Val Pro Cys Val Arg Ala Gly Asn Val Ser Arg Cys 100 105 110

Trp Thr Pro Val Thr Pro Thr Val Ala Ala Val Ser Met Asp Ala Pro 115 120 125

Leu Glu Ser Phe Arg Arg His Val Asp Leu Met Val Gly Ala Ala Thr 130 135 140

Val Cys Ser Val Leu Tyr Val Gly Asp Leu Cys Gly Gly Ala Phe Leu 145 150 155 160

Val Gly Gln Met Phe Thr Phe Gln Pro Arg Arg His Trp Thr Thr Gln 165 170 175

Asp Cys Asn Cys Ser Ile Tyr Thr Gly His Ile Thr Gly His Arg 180 185 190

- (2) INFORMATION FOR SEQ ID NO: 124:
 - (i) SEQUENCE CHARACTERISTICS:
 - (A) LENGTH: 31 base pairs (B) TYPE: nucleic acid
 - (B) TIPE: nucleic acid
 - (C) STRANDEDNESS: single
 (D) TOPOLOGY: linear
 - (ii) MOLECULE TYPE: DNA (genomic)
 - (iii) HYPOTHETICAL: NO
 - (iii) ANTI-SENSE: NO
 - (ix) FEATURE:
 - (A) NAME/KEY: misc_feature
 - (B) LOCATION: 1..31
 - (D) OTHER INFORMATION: /standard name= "HCV Primer HCPr206"
 - (xi) SEQUENCE DESCRIPTION: SEQ ID NO: 124:

TGGGGATCCC GTATGATACC CGCTGCTTTG A

- (2) INFORMATION FOR SEQ ID NO: 125:
 - (i) SEQUENCE CHARACTERISTICS:
 - (A) LENGTH: 30 base pairs
 - (B) TYPE: nucleic acid
 - (C) STRANDEDNESS: single
 - (D) TOPOLOGY: linear
 - (ii) MOLECULE TYPE; DNA (genomic)
 - (iii) HYPOTHETICAL: NO
 - (iii) ANTI-SENSE: YES
 - (ix) FEATURE:
 - (A) NAME/KEY: misc_feature
 - (B) LOCATION: 1..30
 - (D) OTHER INFORMATION: /standard_name= "HCV Primer HcPr207"
 - (xi) SEQUENCE DESCRIPTION: SEQ ID NO: 125:

GGCGGAATTC CTGGTCATAG CCTCCGTGAA

30

31

- (2) INFORMATION FOR SEQ ID NO: 126:
 - (i) SEOUENCE CHARACTERISTICS:
 - (A) LENGTH: 12 amino acids
 - (B) TYPE: amino acid
 - (C) STRANDEDNESS: single
 (D) TOPOLOGY: linear
 - (ii) MOLECULE TYPE: peptide
 - (iii) HYPOTHETICAL: NO
 - (vi) ORIGINAL SOURCE:
 - (A) ORGANISM: amino acid
 - (C) INDIVIDUAL ISOLATE: GB358
 - (xi) SEQUENCE DESCRIPTION: SEQ ID NO: 126:
 - Val Asn Tyr Arg Asn Ala Ser Gly Ile Tyr His Ile 1 5 10
- (2) INFORMATION FOR SEQ ID NO: 127:
 - (i) SEQUENCE CHARACTERISTICS:
 - (A) LENGTH: 12 amino acids
 - (B) TYPE: amino acid
 - (C) STRANDEDNESS: single
 - (D) TOPOLOGY: linear
 - (ii) MOLECULE TYPE: peptide

- (iii) HYPOTHETICAL: NO
- (vi) ORIGINAL SOURCE:
- (A) ORGANISM: Amino acid
 - (C) INDIVIDUAL ISOLATE: GB549
- (xi) SEQUENCE DESCRIPTION: SEQ ID NO: 127:
 - Gln His Tyr Arg Asn Ile Ser Gly Ile Tyr His Val
- (2) INFORMATION FOR SEQ ID NO: 128:
 - (i) SEQUENCE CHARACTERISTICS:
 - (A) LENGTH: 12 amino acids
 - (B) TYPE: amino acid
 - (C) STRANDEDNESS: single (D) TOPOLOGY: linear

 - (ii) MOLECULE TYPE: peptide
 - (iii) HYPOTHETICAL: NO
 - (vi) ORIGINAL SOURCE:
 - (A) ORGANISM: Amino acid
 - (C) INDIVIDUAL ISOLATE: GB809
 - (xi) SEQUENCE DESCRIPTION: SEQ ID NO: 128:
 - Glu His Tyr Arg Asn Ala Ser Gly Ile Tyr His Ile 1 5 10
- (2) INFORMATION FOR SEQ ID NO: 129:
 - (i) SEQUENCE CHARACTERISTICS:
 - (A) LENGTH: 11 amino acids
 - (B) TYPE: amino acid (C) STRANDEDNESS: single
 - (D) TOPOLOGY: linear
 - (ii) MOLECULE TYPE: peptide
 - tan, manager popular
 - (iii) HYPOTHETICAL: NO
 - (vi) ORIGINAL SOURCE:
 - (A) ORGANISM: amino acid
 - (C) INDIVIDUAL ISOLATE: GB358
 - (xi) SEQUENCE DESCRIPTION: SEQ ID NO: 129:
 - Val Tyr Glu Thr Glu His His Ile Leu His Leu 1 5 10
- (2) INFORMATION FOR SEQ ID NO: 130:

- (i) SEQUENCE CHARACTERISTICS:

 (A) LENGTH: 11 amino acids
 - (B) TYPE: amino acid
 - (C) STRANDEDNESS: single
 - (D) TOPOLOGY: linear
- (ii) MOLECULE TYPE: peptide
- (iii) HYPOTHETICAL: NO
- (vi) ORIGINAL SOURCE:
 - (A) ORGANISM: amino acid
 - (C) INDIVIDUAL ISOLATE: GB549
- (xi) SEQUENCE DESCRIPTION: SEO ID NO: 130:
- Val Tyr Glu Ala Asp His His Ile Met His Leu
- (2) INFORMATION FOR SEO ID NO: 131:
 - (i) SEQUENCE CHARACTERISTICS:
 - (A) LENGTH: 11 amino acids
 - (B) TYPE: amino acid
 - (C) STRANDEDNESS: single (D) TOPOLOGY: linear
 - (ii) MOLECULE TYPE: peptide
 - (iii) HYPOTHETICAL: NO
 - (vi) ORIGINAL SOURCE:
 - (A) ORGANISM: amino acid
 - (C) INDIVIDUAL ISOLATE: GB809
 - (xi) SEQUENCE DESCRIPTION: SEQ ID NO: 131:
 - Val Tyr Glu Thr Asp His His Ile Leu His Leu 1 5 10
- (2) INFORMATION FOR SEQ ID NO: 132:
 - (i) SEQUENCE CHARACTERISTICS:
 - (A) LENGTH: 13 amino acids
 - (B) TYPE: amino acid
 - (C) STRANDEDNESS: single (D) TOPOLOGY: linear
 - (ii) MOLECULE TYPE: peptide
 - (iii) HYPOTHETICAL: NO
 - (vi) ORIGINAL SOURCE:
 - (A) ORGANISM: amino acid
 - (C) INDIVIDUAL ISOLATE: GB358

(xi) SEQUENCE DESCRIPTION: SEQ ID NO: 132:

Val Arg Val Gly Asn Gln Ser Arg Cys Trp Val Ala Leu 1 5 10

- (2) INFORMATION FOR SEQ ID NO: 133:
 - (i) SEQUENCE CHARACTERISTICS:
 - (A) LENGTH: 13 amino acids
 - (B) TYPE: amino acid
 - (C) STRANDEDNESS: single
 - (D) TOPOLOGY: linear
 - (ii) MOLECULE TYPE: peptide
 - (iii) HYPOTHETICAL: NO
 - (vi) ORIGINAL SOURCE:
 - (A) ORGANISM: amino acid
 - (C) INDIVIDUAL ISOLATE: GB549
 - (xi) SEQUENCE DESCRIPTION: SEO ID NO: 133:

Val Arg Thr Gly Asn Thr Ser Arg Cys Trp Val Pro Leu 1 5 10

- (2) INFORMATION FOR SEQ ID NO: 134:
 - (i) SEQUENCE CHARACTERISTICS:
 - (A) LENGTH: 13 amino acids
 - (B) TYPE: amino acid
 - (C) STRANDEDNESS: single (D) TOPOLOGY: linear
 - (ii) MOLECULE TYPE: peptide
 - (iii) HYPOTHETICAL: NO
 - (vi) ORIGINAL SOURCE:
 - (A) ORGANISM: amino acid
 - (C) INDIVIDUAL ISOLATE: GB809
 - (xi) SEQUENCE DESCRIPTION: SEQ ID NO: 134:

Val Arg Ala Gly Asn Val Ser Arg Cys Trp Thr Pro Val 1 5 10

- (2) INFORMATION FOR SEQ ID NO: 135:
 - (i) SEQUENCE CHARACTERISTICS:
 - (A) LENGTH: 10 amino ācids
 - (B) TYPE: amino acid
 - (C) STRANDEDNESS: single
 - (D) TOPOLOGY: linear

- (ii) MOLECULE TYPE: peptide /
- (iii) HYPOTHETICAL: NO
- (vi) ORIGINAL SOURCE:
 - (A) ORGANISM: amino acid
 - (C) INDIVIDUAL ISOLATE: GB358
- (xi) SEQUENCE DESCRIPTION: SEQ ID NO: 135:
- Ala Pro Tyr Ile Gly Ala Pro Leu Glu Ser 1 5 10
- (2) INFORMATION FOR SEQ ID NO: 136:
 - (i) SEQUENCE CHARACTERISTICS:
 - (A) LENGTH: 10 amino acids
 - (B) TYPE: amino acid
 - (C) STRANDEDNESS: single (D) TOPOLOGY: linear
 - (ii) MOLECULE TYPE: peptide
 - (iii) HYPOTHETICAL: NO
 - (vi) ORIGINAL SOURCE:
 - (A) ORGANISM: amino acid
 - (C) INDIVIDUAL ISOLATE: GB549
 - (xi) SEQUENCE DESCRIPTION: SEQ ID NO: 136:
 - Ala Pro Tyr Val Gly Ala Pro Leu Glu Ser 1 5 10
- (2) INFORMATION FOR SEO ID NO: 137:
 - (i) SEQUENCE CHARACTERISTICS:
 - (A) LENGTH: 10 amino acids
 - (B) TYPE: amino acid
 - (C) STRANDEDNESS: single
 - (D) TOPOLOGY: linear
 - (ii) MOLECULE TYPE: peptide
 - (iii) HYPOTHETICAL: NO
 - (vi) ORIGINAL SOURCE:
 - (A) ORGANISM: amino acid
 - (C) INDIVIDUAL ISOLATE: GB809
 - (xi) SEQUENCE DESCRIPTION: SEQ ID NO: 137:
 - Ala Val Ser Met Asp Ala Pro Leu Glu Ser 1 5 10
- (2) INFORMATION FOR SEC ID NO: 138:

- (i) SEQUENCE CHARACTERISTICS:
 - (A) LENGTH: 10 amino acids
 - (B) TYPE: amino acid
 - (C) STRANDEDNESS: single (D) TOPOLOGY: linear
- (ii) MOLECULE TYPE: peptide
- (iii) HYPOTHETICAL: NO
- (vi) ORIGINAL SOURCE:
 - - (A) ORGANISM: amino acid (C) INDIVIDUAL ISOLATE: GB358 and GB809
- (xi) SEQUENCE DESCRIPTION: SEO ID NO: 138:

Gln Pro Arg Arg His Trp Thr Thr Gln Asp

- (2) INFORMATION FOR SEQ ID NO: 139:
 - (i) SEQUENCE CHARACTERISTICS:
 - (A) LENGTH: 10 amino acids
 - (B) TYPE: amino acid
 - (C) STRANDEDNESS: single (D) TOPOLOGY: linear
 - (ii) MOLECULE TYPE: peptide
 - (iii) HYPOTHETICAL: NO
 - (vi) ORIGINAL SOURCE: (A) ORGANISM: amino acid
 - (C) INDIVIDUAL ISOLATE: GB549
 - (xi) SEQUENCE DESCRIPTION: SEQ ID NO: 139:

Arg Pro Arg Arg His Trp Thr Thr Gln Asp 5

- (2) INFORMATION FOR SEC ID NO: 140:
 - (i) SEQUENCE CHARACTERISTICS:
 - (A) LENGTH: 10 amino acids
 - (B) TYPE: amino acid
 - (C) STRANDEDNESS: single
 - (D) TOPOLOGY: linear
 - (ii) MOLECULE TYPE: peptide
 - (iii) HYPOTHETICAL: NO
 - (vi) ORIGINAL SOURCE:

24

- (A) ORGANISM: amino acid (C) INDIVIDUAL ISOLATE: GB549
- (xi) SEQUENCE DESCRIPTION: SEO ID NO: 140:

Arg Pro Arg Arg His Trp Thr Thr Gln Asp

- (2) INFORMATION FOR SEC ID NO: 141:
 - (i) SEQUENCE CHARACTERISTICS:
 - (A) LENGTH: 23 base pairs
 - (B) TYPE: nucleic acid (C) STRANDEDNESS: single
 - (D) TOPOLOGY: linear
 - (ii) MOLECULE TYPE: cDNA
 - (iii) HYPOTHETICAL: NO
 - (iii) ANTI-SENSE: NO
 - (xi) SEQUENCE DESCRIPTION: SEO ID NO: 141:

TGGGATATGA TGATGAACTG GTC

(2) INFORMATION FOR SEQ ID NO: 142:

- (i) SEQUENCE CHARACTERISTICS:
 - (A) LENGTH: 24 base pairs
 - (B) TYPE: nucleic acid (D) TOPOLOGY: linear
 - (C) STRANDEDNESS: single
- (ii) MOLECULE TYPE: cDNA
- (iii) HYPOTHETICAL: NO
- (iii) ANTI-SENSE: YES
- (xi) SEQUENCE DESCRIPTION: SEQ ID NO: 142:

CCAGGTACAA CCGAACCAAT TGCC

(2) INFORMATION FOR SEQ ID NO: 143:

- (i) SEQUENCE CHARACTERISTICS:
 - (A) LENGTH: 957 base pairs
 - (B) TYPE: nucleic acid
 - (C) STRANDEDNESS: single
 - (D) TOPOLOGY: linear

160

145

(ii) 1	MOLECULE	TYPE:	CDNA
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- (iii) HYPOTHETICAL: NO
- (iii) ANTI-SENSE: NO

(ix) FEATURE:

- (A) NAME/KEY: CDS
- (B) LOCATION: 1..957

(ix) FEATURE:

- (A) NAME/KEY: mat_peptide
- (B) LOCATION: 1..954

	,	., <u>.</u>	ocni	TON.		J J 4							
(xi) SE	QUEN	CE D	ESCR	IPTI	on:	SEQ	ID N	0: 1	43:			
												AAC Asn	48
												GGT Gly	96
				CCG Pro								GCG Ala	144
				GAG Glu									192
				CGC Arg 70									240
				TAC Tyr									288
				GGG Gly									336
				AAC Asn									384
				ATG Met									432

155

GGT GGT GTC GCC AGA GCT CTC GCG CAT GGC GTG AGA GTT CTG GAA GAC

Gly Gly Val Ala Arg Ala Leu Ala His Gly Val Arg Val Leu Glu Asp

150

(2) INFORMATION FOR SEQ ID NO: 144:

290

305

(i) SEQUENCE CHARACTERISTICS:

310

- (A) LENGTH: 319 amino acids
- (B) TYPE: amino acid
- (D) TOPOLOGY: linear
- (ii) MOLECULE TYPE: protein
- (xi) SEQUENCE DESCRIPTION: SEQ ID NO: 144:

Met Ser Thr Asn Pro Lys Pro Gln Arg Lys Thr Lys Arg Asn Thr Asn

CAA GTC TTC ATC ATC TCG CCC CAG CAT CAT AAG TTT GTC CAG GAC TGC

Gln Val Phe Ile Ile Ser Pro Gln His His Lvs Phe Val Gln Asp Cvs

315

Asn Cys Ser Ile Tyr Pro Gly His Ile Thr Gly His Arg Met Ala

295 AAC TGT TCC ATA TAC CCA GGC CAC ATC ACT GGA CAT CGG ATG GCG 912

957

Arg Arg Pro Gln Asp Val Lys Phe Pro Gly Gly Gly Gln Ile Val Gly 20

- Gly Val Tyr Leu Leu Pro Arg Arg Gly Pro Arg Leu Gly Val Arg Ala 35 40 45
- Thr Arg Lys Thr Ser Glu Arg Ser Gln Pro Arg Gly Arg Arg Gln Pro
- Ile Pro Lys Asp Arg Arg Pro Thr Gly Lys Ser Trp Gly Lys Pro Gly 65 70 75 80
- Tyr Pro Trp Pro Leu Tyr Gly Asn Glu Gly Leu Gly Trp Ala Gly Trp 85 90 95
- Arg His Arg Ser Arg Asn Leu Gly Lys Val Ile Asp Thr Leu Thr Cys \$115\$
- Gly Phe Ala Asp Leu Met Gly Tyr Ile Pro Val Val Gly Ala Pro Val 130 135 140
- Gly Gly Val Ala Arg Ala Leu Ala His Gly Val Arg Val Leu Glu Asp 145 \$150\$
- Gly Ile Asn Tyr Ala Thr Gly Asn Leu Pro Gly Cys Ser Phe Ser Ile 165 170 175
- Phe Leu Leu Ala Leu Leu Ser Cys Ile Thr Val Pro Val Ser Gly Leu 180 185 190
- Gln Val Lys Asn Thr Ser Ser Ser Tyr Met Val Thr Asn Asp Cys Gln 195 200 205
- Asn Ser Ser Ile Val Trp Gln Leu Arg Asp Ala Val Leu His Val Pro 210 215 220
- Gly Cys Val Pro Cys Glu Glu Lys Gly Asn Ile Ser Arg Cys Trp Ile 225 235 240
- Pro Val Ser Pro Asn Ile Ala Val Ser Gln Pro Gly Ala Leu Thr Lys 245 250 255
- Gly Leu Arg Thr His Ile Asp Thr Ile Ile Ala Ser Ala Thr Phe Cys $260 \hspace{1cm} 265 \hspace{1cm} 265 \hspace{1cm} 270 \hspace{1cm}$
- Ser Ala Leu Tyr Ile Gly Asp Leu Cys Gly Ala Val Met Leu Ala Ser 275 280 285
- Gln Val Phe Ile Ile Ser Pro Gln His His Lys Phe Val Gln Asp Cys 290 295 300
- Asn Cys Ser Ile Tyr Pro Gly His Ile Thr Gly His Arg Met Ala $305 \ \ 310 \ \ 315$
- (2) INFORMATION FOR SEQ ID NO: 145:
 - (i) SEQUENCE CHARACTERISTICS:(A) LENGTH: 340 base pairs

(B) TYPE: nucleic acid(C) STRANDEDNESS: single(D) TOPOLOGY: linear

(ii) MOLECULE TYPE: cDNA	
(iii) HYPOTHETICAL: NO	
(iii) ANTI-SENSE: NO	
(ix) FEATURE: (A) NAME/KEY: mat_peptide (B) LOCATION: 2337	
(ix) FEATURE: (A) NAME/KEY: CDS (B) LOCATION: 2340	
(xi) SEQUENCE DESCRIPTION: SEQ ID NO: 145:	
C TCA ACG GTC ACG GAG AGG GAC ATC AGA ACT GAG GAG TCC ATA TAC Ser Thr Val Thr Glu Arg Asp Ile Arg Thr Glu Glu Ser Ile Tyr 1 5 10 15	46
CTT GCT TGC TCT TTA CCC GAG CAG GCA CGG ACT GCC ATA CAC TCA CTG Leu Ala Cys Ser Leu Pro Glu Gln Ala Arg Thr Ala Ile His Ser Leu 20 25 30	94
ACT GAG AGG CTT TAC GTG GGA GGG CCC ATG CTA AAC AGC AAA GGG CAA Thr Glu Arg Leu Tyr Val Gly Gly Pro Met Leu Asn Ser Lys Gly Gln $$35$$ 40 45	142
ACC TGC GGA TAC AGA CGC TGC CGC GGC AGC GGA GTG TTC ACC ACT AGC Thr Cys Gly Tyr Arg Arg Cys Arg Ala Ser Gly Val Phe Thr Thr Ser $50 \\$	190
ATG GGA AAT ACC ATC ACG TGC TAC GTG AAG GCA CAA GCA GCC TGT AAG Met Gly Asn Thr Ile Thr Cys Tyr Val Lys Ala Gln Ala Ala Cys Lys 65 70 75	238
GCT GCG GGC ATA ATT GCC CCC ACG ATG CTG GTG TGC GGC GAC GAT CTA Ala Ala Gly Ile Ile Ala Pro Thr Met Leu Val Cys Gly Asp Asp Leu 80 90 95	286
GTT GTC ATC TCA GAG AGT CAG GGG ACC GAG GAG GAC GAG CGG AAC CTA Val Val Ile Ser Glu Ser Gln Gly Thr Glu Glu Asp Glu Arg Asn Leu 100 105 110	334
CGA GCC Arg Ala	340

- (2) INFORMATION FOR SEQ ID NO: 146:
 - (i) SEQUENCE CHARACTERISTICS:

- (A) LENGTH: 113 amino acids
- (B) TYPE: amino acid (D) TOPOLOGY: linear
- (ii) MOLECULE TYPE: protein
- (xi) SEQUENCE DESCRIPTION: SEQ ID NO: 146:
- Ser Thr Val Thr Glu Arg Asp Ile Arg Thr Glu Glu Ser Ile Tyr Leu
- Ala Cys Ser Leu Pro Glu Gln Ala Arg Thr Ala Ile His Ser Leu Thr
- Glu Arg Leu Tyr Val Gly Gly Pro Met Leu Asn Ser Lys Gly Gln Thr 40
- Cys Gly Tyr Arg Arg Cys Arg Ala Ser Gly Val Phe Thr Thr Ser Met
- Gly Asn Thr Ile Thr Cys Tyr Val Lys Ala Gln Ala Ala Cys Lys Ala 70
- Ala Gly Ile Ile Ala Pro Thr Met Leu Val Cys Gly Asp Asp Leu Val
- Val Ile Ser Glu Ser Gln Gly Thr Glu Glu Asp Glu Arg Asn Leu Arg 100 105

Ala

- (2) INFORMATION FOR SEO ID NO: 147:
 - (i) SEQUENCE CHARACTERISTICS:
 - (A) LENGTH: 345 base pairs
 - (B) TYPE: nucleic acid (D) TOPOLOGY: linear
 - (C) STRANDEDNESS: single
 - (ii) MOLECULE TYPE: cDNA
 - (iii) HYPOTHETICAL: NO
 - (iii) ANTI-SENSE: NO
 - (ix) FEATURE:
 - (A) NAME/KEY: CDS
 - (B) LOCATION: 1..345
 - (ix) FEATURE:
 - (A) NAME/KEY: mat peptide
 - (B) LOCATION: 1..342
 - (xi) SEQUENCE DESCRIPTION: SEQ ID NO: 147:
- ATG AGC ACA CTT CCT AAA CCA CAA AGA AAA ACC AAA AGA AAC ACC AAC

Met 1	Ser	Thr	Leu	Pro 5	Lys	Pro	Gln	Arg	Lys 10	Thr	Lys	Arg	Asn	Thr 15	Asn	
														TTG Leu		. 96
GAG Glu														GTG Val		144
TGC Cys																192

TCC CCA GGG CGC GCC GAA CCG AGG GCA GGT CCT GGG CTC AGC CCG GGT
Ser Pro Gly Arg Ala Glu Pro Arg Ala Gly Pro Gly Leu Ser Pro Gly
70 70 80

ACC CTT GGC CCC TAT ATG GGA ATG AGG GCT GGG GGT GGG CAG GGT GGC
Thr Leu Gly Pro Tyr Met Gly Met Arg Ala Ala Gly Gly Gln Gly Gly
85
90
95

GGC GCA GGA 345 Gly Ala Gly ... 115

- (2) INFORMATION FOR SEQ ID NO: 148:
 - (i) SEQUENCE CHARACTERISTICS:
 - (A) LENGTH: 115 amino acids
 - (B) TYPE: amino acid
 - (D) TOPOLOGY: linear
 - (ii) MOLECULE TYPE: protein

(xi) SEQUENCE DESCRIPTION: SEQ ID NO: 148: Met Ser Thr Leu Pro Lys Pro Gln Arg Lys Thr Lys Arg A

Met Ser Thr Leu Pro Lys Pro Gln Arg Lys Thr Lys Arg Asn Thr Asn $1 \hspace{1.5cm} 5 \hspace{1.5cm} 10 \hspace{1.5cm} 15$

Pro Gly His Arg Thr Leu Ser Ser Gln Ala Ala Val Arg Ser Leu Val 20 25 30

Glu Phe Thr Cys Tyr His Ala Gly Ala Pro Ser Trp Val Cys Val Gln
35 40 45

Cys Ala Arg Leu Pro Ser Gly Arg Asn Leu Ala Val Gly Ala Asn Pro $50 \hspace{1cm} 55 \hspace{1cm} 60$

Ser Pro Gly Arg Ala Glu Pro Arg Ala Gly Pro Gly Leu Ser Pro Gly

Thr Leu Gly Pro Tyr Met Gly Met Arg Ala Ala Gly Gly Gln Gly Gly

	85	90	95	
	rg Ala Ala Leu Ala 00	Arg Arg Gly Ala 105	Gln Met Thr Pro	
Gly Ala Gly 115				
(2) INFORMATIO	ON FOR SEQ ID NO:	149:	-	
(A) (B) (C)	ENCE CHARACTERISTI LENGTH: 280 base TYPE: nucleic aci STRANDEDNESS: sin TOPOLOGY: linear	pairs d		
(ii) MOLEC	CULE TYPE: CDNA			
	NAME/KEY: CDS			
(B)	LOCATION: 2280			
	RE: NAME/KEY: mat_pept LOCATION: 2277	tide		
(xi) SEQUE	NCE DESCRIPTION: 5	SEQ ID NO: 149:		
G GCC TGT GAC	CTC AAG GAC GAG GO Leu Lys Asp Glu Al	T AGG AGG GTG AT		46
G GCC TGT GAC Ala Cys Asp 1 ACG GAG CGG CT	CTC AAG GAC GAG GC Leu Lys Asp Glu Al	TT AGG AGG GTG AT La Arg Arg Val II 10 CCT ATG TTC AAC	e Thr Ser Leu 15 AGC AAG GGA CAA	4 6
G GCC TGT GAC Ala Cys Asp 1 ACG GAG CGG CT Thr Glu Arg Le CAC TGC GGT TA	CTC AAG GAC GAG GC Leu Lys Asp Glu Al 5 T TAC TGT GGT GGT u Tyr Cys Gly Gly 20 C CGC CGC TGC CGT r Arg Arg Cys Arg	T AGG AGG GTG AT LA Arg Arg Val II 10 CCT ATG TTC AAC Pro Met Phe Asn 25 GCT AGT GGG GTG	e Thr Ser Leu 15 AGC AAG GGA CAA Ser Lys Gly Gln 30 CTA CCC ACC AGC	
G GCC TGT GAC Ala Cys Asp 1 ACG GAG CGG CT Thr Glu Arg Le CAC TGC GGT TA His Cys Gly Ty 3 TTC GGG AAC AC	CTC AAG GAC GAG GC Leu Lys Asp Glu Al 5 T TAC TGT GGT GGT u Tyr Cys Gly Gly 20 C CGC CGC TGC CGT r Arg Arg Cys Arg	T AGG AGG GTG AT LE ARG ARG VAL 11 10 CCT ATG TTC AAC Pro Met Phe Asn 25 GCT AGT GGG GTG Ala Ser Gly Val 40 ATC AAA GCA AAG	e Thr Ser Leu 15 AGC AAG GGA CAA Ser Lys Gly Gln 30 CTA CCC ACC AGC Leu Pro Thr Ser 45 GCA GCT ACC AAA	94
G GCC TGT GAC Ala Cys Asp 1 ACG GAG GGG CT Thr Glu Arg Le CAC TGC GGT TA His Cys Gly Ty 3 TTC GGG AAC AC Phe Gly Asn Th 50 GCT GCC GGA AT	CTC AAG GAC GAG GG Leu Lys Asp Glu Al T TAC TGT GGT GGT U Tyr Cys Gly Gly 20 C CGC CGC TGC CGT r Arg Arg Cys Arg 5 A ATC ACC TGT TAC r Ile Thr Cys Tyr	TAGE AGE GTE AT LA ARG ATG TTC AAC PTC MET PHE ASN 25 GGE GTE ALA SET GLY VA1 40 ATC AAA GCA AAG ILE LYS ALA LYS TTC CTT GTC TGC TGC	e Thr Ser Leu 15 AGC AAG GGA CAA Ser Lys Gly Gln 30 CTA CCC AGC AGC Leu Pro Thr Ser 45 GCA GCT ACC AAA Ala Ala Thr Lys 60 GGA GAT GAC TTG	94 142
G GCC TGT GAC Ala Cys Asp 1 ACG GAG GGG CT Thr Glu Arg Le CAC TGC GGT TA His Cys Gly Ty 3 TTC GGG AAC AC Phe Gly Asn Th 50 GCT GCC GGA AT Ala Ala Gly Tl 65 GTC GTC GTC ATT GC	CTC AAG GAC GAG GG Leu Lys Asp Glu Al T TAC TGT GGT GGT u Tyr Cys Gly Gly 20 C CGC CGC TGC CGT r Arg Arg Cys Arg 5 A ATC ACC TGT TAC r Ile Thr Cys Tyr T AAA AAT CCA TGA e Lys Asp Pro Ser	TAGG AGG GTG AT LA ARG ARG ATG TTC AAC PTO MET PHE ASN 25 GGG GTG ALA SET GLY VAI 40 ATC AAA GCA AAG ILE LYS ALA LYS TTC CTT GTC TGC PHE LEU VAI CYS ATC GAT GAG GAC GAC GAT GAG GAC GAC GAT GAG GAC AGG GAC AGG AGG AGG AGG AGG AGG	e Thr Ser Leu 15 AGC AAG GGA CAA Ser Lys Gly Gln 30 CTA CCC ACC AGC Leu Pro Thr Ser 45 GCA GGT ACC AAA Haa Ala Thr Lys 60 GGA GAT GAC TTG GIy Asp Asp Leu AGA GCG	94 142 190

(i) SEQUENCE CHARACTERISTICS: (A) LENGTH: 93 amino acids

- (B) TYPE: amino acid
- (D) TOPOLOGY: linear
- (ii) MOLECULE TYPE: protein
- (xi) SEQUENCE DESCRIPTION: SEQ ID NO: 150;
- Ala Cys Asp Leu Lys Asp Glu Ala Arg Arg Val Ile Thr Ser Leu Thr
- Glu Arg Leu Tyr Cys Gly Gly Pro Met Phe Asn Ser Lys Gly Gln His
- Cys Gly Tyr Arg Arg Cys Arg Ala Ser Gly Val Leu Pro Thr Ser Phe
- Gly Asn Thr Ile Thr Cys Tyr Ile Lys Ala Lys Ala Ala Thr Lys Ala
- Ala Gly Ile Lys Asn Pro Ser Phe Leu Val Cys Gly Asp Asp Leu Val
- Val Ile Ala Glu Ser Ala Gly Ile Asp Glu Asp Arg Ala 85
- (2) INFORMATION FOR SEO ID NO: 151:
 - (i) SEQUENCE CHARACTERISTICS:
 - (A) LENGTH: 499 base pairs
 - (B) TYPE: nucleic acid
 - (C) STRANDEDNESS: single (D) TOPOLOGY: linear
 - (ii) MOLECULE TYPE: cDNA
 - (iii) HYPOTHETICAL: NO
 - (iii) ANTI-SENSE: NO
 - (ix) FEATURE:
 - (A) NAME/KEY: CDS
 - (B) LOCATION: 1..499
 - (ix) FEATURE:
 - (A) NAME/KEY: mat peptide
 - (B) LOCATION: 1..496
 - (xi) SEQUENCE DESCRIPTION: SEQ ID NO: 151:
- ATG AGC ACG AAT CCT AAA CCT CAA AGA AAA ACC AAA AGA AAC ACC AAC Met Ser Thr Asn Pro Lys Pro Gln Arg Lys Thr Lys Arg Asn Thr Asn
- CGT CGC CCA CAG GAC GTC AAG TTC CCG GGC GGT GGT CAG ATC GTT GGC Arg Arg Pro Gln Asp Val Lys Phe Pro Gly Gly Gly Gln Ile Val Gly 20 25

•	'n	4	

GTT Val									144
CGG Arg 50									192
CCC Pro									240
CCT Pro									288
CTC Leu									336
CGA Arg									384
TTC Phe 130									432
ggc Gly									480
GTA Val	Tyr		G						499

- (2) INFORMATION FOR SEQ ID NO: 152:
 - (i) SEQUENCE CHARACTERISTICS:
 - (A) LENGTH: 166 amino acids
 - (B) TYPE: amino acid
 - (D) TOPOLOGY: linear
 - (ii) MOLECULE TYPE: protein
 - (xi) SEQUENCE DESCRIPTION: SEQ ID NO: 152:

Met Ser Thr Asn Pro Lys Pro Gln Arg Lys Thr Lys Arg Asn Thr Asn 1 $$ 15

Arg Arg Pro Gln Asp Val Lys Phe Pro Gly Gly Gly Gln Ile Val Gly $20 \ \ 25 \ \ 30$

Gly Val Tyr Leu Leu Pro Arg Arg Gly Pro Arg Met Gly Val Arg Ala 35 40 45

96

Thr Arg Lys Thr Ser Glu Arg Ser Gln Pro Arg Gly Arg Arg Gln Pro 50 55 60

Ile Pro Lys Ala Arg Gln Pro Thr Gly Arg Ser Trp Gly Gln Pro Gly 65 70 75 80

Tyr Pro Trp Pro Leu Tyr Ala Asn Glu Gly Leu Gly Trp Ala Gly Trp 85 90 95

Leu Leu Ser Pro Arg Gly Ser Arg Pro Asn Trp Gly Pro Asn Asp Pro 100 105 110

Arg Arg Lys Ser Arg Asn Leu Gly Lys Val Ile Asp Thr Leu Thr Cys 115 120 125

Gly Phe Ala Asp Leu Met Gly Tyr Ile Pro Leu Val Gly Gly Pro Ile 130 135 140 Gly Gly Val Ala Arg Ala Leu Ala His Gly Val Arg Val Leu Glu Asp 145 150 155 160

Gly Val Asn Tyr Ala Thr

- (2) INFORMATION FOR SEQ ID NO: 153:
 - (i) SECUENCE CHARACTERISTICS:
 - (A) LENGTH: 579 base pairs
 - (B) TYPE: nucleic acid
 - (C) STRANDEDNESS: single
 - (D) TOPOLOGY: linear
 - (ii) MOLECULE TYPE: cDNA
 - (iii) HYPOTHETICAL: NO
 - (iii) ANTI-SENSE: NO
 - (ix) FEATURE:
 - (A) NAME/KEY: CDS
 - (B) LOCATION: 1..579
 - (ix) FEATURE:
 - (A) NAME/KEY: mat_peptide
 - (B) LOCATION: 1..576
 - (xi) SEQUENCE DESCRIPTION: SEQ ID NO: 153:

ACG TGC GGA TTC GCC GAT CTC ATG GGG TAC ATC CCG CTC GTA GGC GGC Thr Cys Gly Phe Ala Asp Leu Met Gly Tyr Ile Pro Leu Val Gly Gly

CCC GTT GGG GGC GTC GCA AGG GCT CTC GCA CAC GGT GTG AGG GTC CTT Prc Val Gly Gly Val Ala Arg Ala Leu Ala His Gly Val Arg Val Leu 20 25 30

GAG GAC GGG GTA AAC TAT CCA ACA GGG AAT TTA CCC GGT TGC TCT TTC 144

WO 94/25601

Glu	Asp	Gly 35	Val	Asn	Tyr	Pro	Thr 40	Gly	Asn	Leu	Pro	Gly 45	Cys	Ser	Phe	
						CTT Leu 55										192
						GCC Ala										240
						GTC Val										288
						TGT Cys										336
						ACA Thr										384
						GCC Ala 135										432
						GTA Val									TTG Leu 160	480
						TAT Tyr										528
AAC Asn																576
GCG Ala																579

- (2) INFORMATION FOR SEQ ID NO: 154:
 - (i) SEQUENCE CHARACTERISTICS:
 - (A) LENGTH: 193 amino acids
 - (B) TYPE: amino acid (D) TOPOLOGY: linear

 - (ii) MOLECULE TYPE: protein
 - (xi) SEQUENCE DESCRIPTION: SEQ ID NO: 154:

Thr Cys Gly Phe Ala Asp Leu Met Gly Tyr Ile Pro Leu Val Gly Gly 15 1 5 10

Pro Val Gly Gly Val Ala Arg Ala Leu Alá His Gly Val Arg Val Leu 20 25 30

Glu Asp Gly Val Asn Tyr Pro Thr Gly Asn Leu Pro Gly Cys Ser Phe 35 40 45

Ser Ile Phe Ile Leu Ala Leu Leu Ser Cys Leu Thr Val Pro Ala Ser 50 55 60

Ala Val Pro Tyr Arg Asn Ala Ser Gly Ile Tyr His Val Thr Asn Asp 65 70 75 80

Cys Pro Asn Ser Ser Ile Val Tyr Glu Ala Asp Asn Leu Ile Leu His $85 \hspace{1.5cm} 90 \hspace{1.5cm} 95$

Ala Pro Gly Cys Val Pro Cys Val Met Thr Gly Asn Val Ser Arg Cys
100 105 110

Trp Val Gln Ile Thr Pro Thr Leu Ser Ala Pro Ser Leu Gly Ala Val \$115\$ \$120\$

Thr Ala Pro Leu Arg Arg Ala Val Asp Tyr Leu Ala Gly Gly Ala Ala 130 \$135\$

Leu Cys Ser Ala Leu Tyr Val Gly Asp Ala Cys Gly Ala Leu Phe Leu 145 150 155 160

Val Gly Gln Met Phe Thr Tyr Arg Pro Arg Gln His Ala Thr Val Gln 165 170 175

Asn Cys Asn Cys Ser Ile Tyr Ser Gly His Val Thr Gly His Arg Met 180 185 190

Ala

- (2) INFORMATION FOR SEQ ID NO: 155:
 - (i) SEQUENCE CHARACTERISTICS:
 - (A) LENGTH: 579 base pairs
 - (B) TYPE: nucleic acid
 - (C) STRANDEDNESS: single
 - (D) TOPOLOGY: linear
 - (ii) MOLECULE TYPE: cDNA
 - (iii) HYPOTHETICAL: NO
 - (iii) ANTI-SENSE: NO
 - (ix) FEATURE:
 - (A) NAME/KEY: CDS
 - (B) LOCATION: 1..579
 - (ix) FEATURE:
 - (A) NAME/KEY: mat peptide
 - (B) LOCATION: 1..576

(xi) SEQUENCE DESCRIPTION: SEQ ID NO: 155:

ACG	TGC	GGA	TTC	GCC	GAC	CTC	GTG	GGG	TAC	ATC	CCG	CTC	GTA	GGC	GGC	48
Thr	Cys	Gly	Phe	Ala	Asp	Leu	Val	Gly	Tyr	Ile	Pro	Leu	Val	Gly	Gly	
1				5					10					15		

	GAC Asp																144
--	------------	--	--	--	--	--	--	--	--	--	--	--	--	--	--	--	-----

	ATC															
Ser	Ile 50	Phe	Ile	Leu	Ala	Leu 55	Leu	Ser	Cys	Leu	Thr 60	Val	Pro	Ala	Ser	
	30					55					60					

Ala Val Pro Tyr Arg Asn Ala Ser Gly Ile Tyr His Val Thr Asn Asp	
65 70 75 80	

TGC CCA AAC T	CT TCC ATA GI	TAT GAG GCA GAT	GAT CTG ATC CTA	CAC 288
Cys Pro Asn S	Ser Ser Ile Va	Tyr Glu Ala Asp	Asp Leu Ile Leu	His
	85	90	95	

GCA	CCT	GGC	TGC	GTG	CCT	TGT	GTC	AGG	AAA	GAT	AAT	GTG	AGT	AGG	TGC	336
Ala	Pro	Gly	Cys	Val	Pro	Cys	Val	Arg	Lys	Asp	Asn	Val	Ser	Arg	Cys	
			100					105					110			

TGG	GTC	CAA	ATT	ACC	CCC	ACG	CTG	TCA	GCC	CCG	AGC	TTC	GGA	GCA	GTC	384
Trp	Val	Gln	Ile	Thr	Pro	Thr	Leu	Ser	Ala	Pro	Ser	Phe	Gly	Ala	Val	
		115					120					125				

ACC	GCT	CCC	CTT	CGG	AGA	GCC	GTT	GAT	TAC	TTG	GTG	GGA	GGG	GCT	GCC	432
Thr	Ala	Pro	Leu	Arg	Arg	Ala	Val	Asp	Tyr	Leu	Val	Gly	Gly	Ala	Ala	
	130					135					140					

	CTC	TGC	TCC	GCG	TTA	TAC	GTT	GGA	GAC	GCG	TGT	GGG	GCA	CTA	$\mathbf{T}\mathbf{T}\mathbf{T}$	TTG	480
1	Leu	Cys	Ser	Ala	Leu	Tyr	Val	Gly	Asp	Ala	Cys	Gly	Ala	Leu	Phe	Leu	
	L45					150					155					160	

GTA	GGC	CAA	ATG	TTC	ACC	TAT	AGG	CCT	CGC	CAG	CAT	GCT	ACG	GTG	CAG	5	28
	Gly																
val	GTA	GIII	Mec		1111	TYL	ALG	FIG		GIII	nis	ALA	TIIL		GILL		
				165					170					175			

GAC	TGC	AAC	TGT	TCC	ATC	TAC	AGT	GGC	CAC	GTC	ACC	GGC	CAT	CAG	ATG	576
Asp	Cys	Asn	Cys	Ser	Ile	Tyr	Ser	Gly	His	Val	Thr	Gly	His	Gln	Met	
			180					185					190			

GCA	579
*1 -	

⁽²⁾ INFORMATION FOR SEQ ID NO: 156:

- (i) SEQUENCE CHARACTERISTICS:
 - (A) LENGTH: 193 amino acids
 - (B) TYPE: amino acid
 - (D) TOPOLOGY: linear
- (ii) MOLECULE TYPE: protein
- (xi) SEQUENCE DESCRIPTION: SEQ ID NO: 156:

Thr Cys Gly Phe Ala Asp Leu Val Gly Tyr Ile Pro Leu Val Gly Gly

1 5 10 15

Pro Val Gly Gly Val Ala Arg Ala Leu Ala His Gly Val Arg Val Leu $20 \hspace{1cm} 25 \hspace{1cm} 30$

Glu Asp Gly Val Asn Tyr Ala Thr Gly Asn Leu Pro Gly Cys Ser Phe $35 \ 40 \ 45$

Ser Ile Phe Ile Leu Ala Leu Leu Ser Cys Leu Thr Val Pro Ala Ser 50 55 60

Ala Val Pro Tyr Arg Asn Ala Ser Gly Ile Tyr His Val Thr Asn Asp 65 70 75 80

Cys Pro Asn Ser Ser Ile Val Tyr Glu Ala Asp Asp Leu Ile Leu His 85 90 95

Ala Pro Gly Cys Val Pro Cys Val Arg Lys Asp Asn Val Ser Arg Cys
100 105 110

Trp Val Gln Ile Thr Pro Thr Leu Ser Ala Pro Ser Phe Gly Ala Val

Thr Ala Pro Leu Arg Arg Ala Val Asp Tyr Leu Val Gly Gly Ala Ala 130 135 140

Val Gly Gln Met Phe Thr Tyr Arg Pro Arg Gln His Ala Thr Val Gln 165 170 175

Asp Cys Asn Cys Ser Ile Tyr Ser Gly His Val Thr Gly His Gln Met 180 \$180\$

Ala

- (2) INFORMATION FOR SEO ID NO: 157:
 - (i) SEQUENCE CHARACTERISTICS:
 - (A) LENGTH: 530 base pairs (B) TYPE: nucleic acid
 - (C) STRANDEDNESS: single
 - (D) TOPOLOGY: linear
 - (ii) MOLECULE TYPE: cDNA
 - (11) 110200000 11141 00111

,	HYPOTHETICAL:	MO		

- (iii) ANTI-SENSE: NO

(ix) FEATURE:

(A) NAME/KEY: CDS

(B) LOCATION: 3..530

(ix) FEATURE:

(A) NAME/KEY: mat_peptide

(B) LOCATION: 3..527

(xi) SEQUENCE DESCRIPTION: SEQ ID NO: 157:

Ala Ala Tyr Tyr Ala Ser Val Ala Asn Trp Thr Lys Val Val Leu Val
35 40 45

TTG TTT CTG TTT GCA GGG GTT GAT GCT ACT ACC CAG ATT TCG GGC GGC 191

Leu Phe Leu Phe Ala Gly Val Asp Ala Thr Thr Gln Ile Ser Gly Gly 50 60

TCC AGC GCC CAA ACG ACG TAT GGC ATC GCC TCA TTT ATC ACC CGC GGC 239 Ser Ser Ala Gln Thr Thr Tyr Gly Ile Ala Ser Phe Ile Thr Arg Gly 65 70 75

GCG CAG CAG AAA CTG CAG CTC ATA AAT ACC AAC GGA AGC TGG CAC ATC
Ala Gln Gln Lys Leu Gln Leu Ile Asn Thr Asn Gly Ser Trp His Ile
80 85 90 95

AAC AGG ACC GCC CTT AAT TOT AAT GAC AGC CTC CAG ACT GGG TTC ATA 335
Asn Arg Thr Ala Leu Asn Cys Asn Asp Ser Leu Gln Thr Gly Phe Ile
100 105 110

GCC GGC CTC TTC TAC TAC CAT AAG TTC AAC TCT TCT GGA TGC CCG GAT
Ala Gly Leu Phe Tyr Tyr His Lys Phe Asn Ser Ser Gly Cys Pro Asp
115
120
125

CGG ATG GCT AGC TGT AGG GCC CTT GCC ACT TTT GAC CAG GGC TGG GGA
Arg Met Ala Ser Cys Arg Ala Leu Ala Thr Phe Asp Gln Gly Trp Gly

ACT ATC AGC TAT GCC AAC ATA TCG GGT CCC AGT GAT GAC AAA CCA TAT
Thr Ile Ser Tyr Ala Asm Ile Ser Gly Pro Ser Asp Asp Lys Pro Tyr
145
150
150
155

TGC TGG CAC TAT CCC CCA CGG CCG TGC GGA GTG GTG CCA GCC CAA GAG

Cys Trp His Tyr Pro Pro Arg Pro Cys Gly Val Val Pro Ala Gln Glu 160 165 170 170

GTC Val 530

- (2) INFORMATION FOR SEQ ID NO: 158:
 - (i) SEQUENCE CHARACTERISTICS:
 - (A) LENGTH: 176 amino acids
 - (B) TYPE: amino acid
 (D) TOPOLOGY: linear
 - (ii) MOLECULE TYPE: protein
 - (xi) SEQUENCE DESCRIPTION: SEQ ID NO: 158:

Pro Thr Thr Ala Leu Leu Val Ala Gln Leu Leu Arg Ile Pro Gln Val

Val Ile Asp Ile Ile Ala Gly Ser His Trp Gly Val Leu Phe Ala Ala 20 25 30

Ala Tyr Tyr Ala Ser Val Ala Asn Trp Thr Lys Val Val Leu Val Leu $35 \hspace{1cm} 40 \hspace{1cm} 45$

Phe Leu Phe Ala Gly Val Asp Ala Thr Thr Gln Ile Ser Gly Gly Ser 50 60

Ser Ala Gln Thr Thr Tyr Gly Ile Ala Ser Phe Ile Thr Arg Gly Ala 65 75 80

Gln Gln Lys Leu Gln Leu Ile Asn Thr Asn Gly Ser Trp His Ile Asn 85 90 95

Arg Thr Ala Leu Asn Cys Asn Asp Ser Leu Gln Thr Gly Phe Ile Ala 100 105 110

Gly Leu Phe Tyr Tyr His Lys Phe Asn Ser Ser Gly Cys Pro Asp Arg 115 120 125

Met Ala Ser Cys Arg Ala Leu Ala Thr Phe Asp Gln Gly Trp Gly Thr 130 135 140

Ile Ser Tyr Ala Asn Ile Ser Gly Pro Ser Asp Asp Lys Pro Tyr Cys 145 150 155 160

Trp His Tyr Pro Pro Arg Pro Cys Gly Val Val Pro Ala Gln Glu Val
165 170 175

- (2) INFORMATION FOR SEQ ID NO: 159:
 - (i) SEQUENCE CHARACTERISTICS:
 - (A) LENGTH: 340 base pairs
 - (B) TYPE: nucleic acid
 - (C) STRANDEDNESS: single

1-1	TOPOLOGY:	7 4

- (ii) MOLECULE TYPE: cDNA
- (iii) HYPOTHETICAL: NO
- (iii) ANTI-SENSE: NO
- (ix) FEATURE:
 - (A) NAME/KEY: CDS
 - (B) LOCATION: 2..340
- (ix) FEATURE:
 - (A) NAME/KEY: mat_peptide
 - (B) LOCATION: 2..337
- (xi) SEQUENCE DESCRIPTION: SEQ ID NO: 159:
- C TCG ACC GTT ACC GAA CAT GAC ATA ATG ACC GAA GAG TCC ATT TAC 46 Ser Thr Val Thr Glu His Asp Ile Met Thr Glu Glu Ser Ile Tyr
- CAA TCA TGT GAC TTG CAG CCC GAG GCA CGC GCA GCA ATA CGG TCA CTC Gln Ser Cys Asp Leu Gln Pro Glu Ala Arg Ala Ala Ile Arg Ser Leu
- ACC CAA CGC CTC TAC TGT GGA GGC CCC ATG TAC AAC AGC AAG GGG CAA 142 Thr Gln Arg Leu Tyr Cys Gly Gly Pro Met Tyr Asn Ser Lys Gly Gln 40
- CAG TGT GGT TAT CGC AGA TGC CGC GCC AGC GGC GTT TTC ACC ACC AGT 190 Gln Cys Gly Tyr Arg Arg Cys Arg Ala Ser Gly Val Phe Thr Thr Ser
- ATG GGC AAC ACC ATG ACG TGC TAC ATC AAG GCT TTA GCC TCC TGT AGA 238 Met Gly Asn Thr Met Thr Cys Tyr Ile Lys Ala Leu Ala Ser Cys Arg 70
- GCC GCA AGG CTC CGG GAC TGC ACG CTC CTG GTG TGT GGT GAC GAT CTT 286 Ala Ala Arg Leu Arg Asp Cys Thr Leu Leu Val Cys Gly Asp Asp Leu 80 85
- GTG GCC ATC TGC GAG AGC CAG GGG ACA CAC GAG GAT GAA GCA AGC CTG 334 Val Ala Ile Cys Glu Ser Gln Gly Thr His Glu Asp Glu Ala Ser Leu 100 105

AGA GCC 340 Arg Ala

- (2) INFORMATION FOR SEO ID NO: 160:
 - (i) SEQUENCE CHARACTERISTICS:
 - (A) LENGTH: 113 amino acids
 - (B) TYPE: amino acid

(D) TOPOLOGY: linear

- (ii) MOLECULE TYPE: protein
- (xi) SEQUENCE DESCRIPTION: SEQ ID NO: 160:

Ser Thr Val Thr Glu His Asp Ile Met Thr Glu Glu Ser Ile Tyr Gln

Ser Cys Asp Leu Gln Pro Glu Ala Arg Ala Ala Ile Arg Ser Leu Thr 20 25 30

Gln Arg Leu Tyr Cys Gly Gly Pro Met Tyr Asn Ser Lys Gly Gln Gln 35 40 45

Cys Gly Tyr Arg Arg Cys Arg Ala Ser Gly Val Phe Thr Thr Ser Met 50 55 60

Gly Asn Thr Met Thr Cys Tyr Ile Lys Ala Leu Ala Ser Cys Arg Ala 65 70 75 80

Ala Arg Leu Arg Asp Cys Thr Leu Leu Val Cys Gly Asp Asp Leu Val 85 90 95

Ala Ile Cys Glu Ser Gln Gly Thr His Glu Asp Glu Ala Ser Leu Arg 100 105 110

Ala

- (2) INFORMATION FOR SEQ ID NO: 161:
 - (i) SEQUENCE CHARACTERISTICS:
 - (A) LENGTH: 340 base pairs (B) TYPE: nucleic acid
 - (C) STRANDEDNESS: single
 - (D) TOPOLOGY: linear
 - (ii) MOLECULE TYPE: cDNA
 - (iii) HYPOTHETICAL: NO
 - (iii) ANTI-SENSE: NO
 - (ix) FEATURE:
 - (A) NAME/KEY: CDS (B) LOCATION: 2..340
 - (ix) FEATURE:
 - (A) NAME/KEY: mat_peptide
 (B) LOCATION: 2..337
 - B) DOCALION: 2...33
 - (xi) SEQUENCE DESCRIPTION: SEQ ID NO: 161:
- C TCA ACC GCC ACC GAA CAT GAC ATA TTG ACT GAA GAG TCC ATA TAC Ser Thr Ala Thr Glu His Asp Ile Leu Thr Glu Glu Ser Ile Tyr

WO 94	/2560	1						2	11						PCT/I	EP94/01323
	1				5					10					15	
															CTC Leu	. 1
	CAA Gln														CAA Gln	142
	TGT Cys														AGT Ser	190
	GGC Gly 65															238
	GCT Ala															286
	GCC Ala															334
AGA Arg																340
(2)	INFO	RMAI	NOI	FOR	SEQ	ID 1	io: 1	L62:								
	((Z) LE	NGTI PE:	CHAF I: 11 amir GY:	.3 an	nino cid									
	(ii)	MOL	ECUI	E T	PE:	prot	ein									
	(xi)	SEÇ	UENC	E DI	SCRI	PTIC	N: S	EQ 1	D NO): 16	2:					
Ser 1	Thr	Ala	Thr	Glu 5	His	Asp	Ile	Leu	Thr 10	Glu	Glu	Ser	Ile	Tyr 15	Gln	
Ser	Cys	Asp	Ser 20	Gln	Pro	Asp	Ala	Arg 25	Ala	Ala	Ile	Arg	Ser 30	Leu	Thr	
Gln	Arg	Leu 35	Phe	Cys	Gly	Gly	Pro 40	Met	Tyr	Asn	Ser	Lys 45	Gly	Gln	Gln	

Cys Gly Tyr Arg Arg Cys Arg Ala Ser Gly Val Phe Thr Thr Ser Met 50 60 810 Asn Thr Met Thr Cys Tyr Ile-Lys Ala Leu Ala Ser Cys Arg Thr 65 70 80 Ala Gly Leu Arg Asp Tyr Thr Leu Leu Val Cys Gly Asp Asp His Val 85 90 95

Ala Ile Cys Glu Ser Gln Gly Thr His Glu Asp Glu Ala Asn Leu Arg 100 $$105\$

Ala

(2)	INFORMATION	FOR	SEO	TD	NO:	163:

(i) SEQUENCE CHARACTERISTICS:

- (A) LENGTH: 499 base pairs
- (B) TYPE: nucleic acid
- (C) STRANDEDNESS: single
- (D) TOPOLOGY: linear

(ii) MOLECULE TYPE: cDNA

- (iii) HYPOTHETICAL: NO
- (iii) ANTI-SENSE: NO

(ix) FEATURE:

- (A) NAME/KEY: CDS
- (B) LOCATION: 1..499

(ix) FEATURE:

- (A) NAME/KEY: mat_peptide
- (B) LOCATION: 1..496

(xi) SEQUENCE DESCRIPTION: SEQ ID NO: 163:

ATG	AGC	ACG	AAT	CCT	AAA	CTT	CAA	AGA	AAA	ACC	AAA	CGT	AAC	ACC	AAC	48
Met	Ser	Thr	Asn	Pro	Lys	Leu	Gln	Arg	Lys	Thr	Lys	Arg	Asn	Thr	Asn	
1				5					10					15		

CGC	CGC	CCC	ATG	GAC	GTT	AAG	TTC	CCG	GGT	GGT	GGC	CAG	ATC	GTT	GGC	96
Arg	Arg	Pro	Met	Asp	Val	Lys	Phe	Pro	Gly	Gly	Gly	Gln	Ile	Val	Gly	
			20					25					30			

GGA GTT	TAC	TTG	TTG	CCG	CGC	AGG	GGC	CCT	AGG	TTG	GGT	GTG	CGC	GCG	1.	44
Gly Val	Tyr	Leu	Leu	Pro	Arg	Arg	Gly	Pro	Arg	Leu	Gly	Val	Arg	Ala		
	2.5					40					4 5					

ACT	CGG	AAG	ACT	TCG	GAG	CGG	TCG	CAA	CCT	CGT	GGG	AGG	CGC	CAA	CCT	192
Thr	Arg	Lys	Thr	Ser	Glu	Arg	Ser	Gln	Pro	Arg	Gly	Arg	Arg	Gln	Pro	
	E 0										60					

ATC	CCC	AAG	GCG	CGC	CGA	TCC	GAG	GGC	AGA	TCC	TGG	GCG	CAG	CCC	GGG	240
															Gly	
65					70			•	_	75	-				80	

TAT	CCT	TGG	CCC	CTT	TAC	GGC	AAT	-GAG	GGC	TGT	GGG	TGG	GCA	GGG	TGG-	288
Tyr	Pro	Trp	Pro	Leu	Tyr	Gly	Asn	Glu	Gly	Cys	Gly	Trp	Ala	Gly	Trp	
				85					90					95		

CTC CTG TCC CCT CGC GGG TCT CGG CCG TCT TGG GGC CCT AAT GAT CCC

165
(2) INFORMATION FOR SEO ID NO: 164:

Gly Ile Asn Tyr Ala Thr

- (i) SEQUENCE CHARACTERISTICS:
 - (A) LENGTH: 166 amino acids
 - (B) TYPE: amino acid (D) TOPOLOGY: linear
- (ii) MOLECULE TYPE: protein
- (xi) SEQUENCE DESCRIPTION: SEQ ID NO: 164:

Met Ser Thr Asn Pro Lys Leu Gln Arg Lys Thr Lys Arg Asn Thr Asn

Arg Arg Pro Met Asp Val Lys Phe Pro Gly Gly Gly Gln Ile Val Gly 20 25 30

Gly Val Tyr Leu Leu Pro Arg Arg Gly Pro Arg Leu Gly Val Arg Ala

Thr Arg Lys Thr Ser Glu Arg Ser Gln Pro Arg Gly Arg Arg Gln Pro $50 \ \ \, 55 \ \ \, 60$

Ile Pro Lys Ala Arg Arg Ser Glu Gly Arg Ser Trp Ala Gln Pro Gly 65 70 75 80

Tyr Pro Trp Pro Leu Tyr Gly Asn Glu Gly Cys Gly Trp Ala Gly Trp 85 90 95

Leu Leu Ser Pro Arg Gly Ser Arg Pro Ser Trp Gly Pro Asn Asp Pro 100 105 110

Arg Arg Arg Ser Arg Asn Leu Gly Lys Val Ile Asp Thr Leu Thr Cys \$115\$ $$120\,^{-}$$ \$125\$

Gly Phe Ala Asp Leu Met Gly Tyr Ile Pro Leu Val Gly Ala Pro Val

Gly	Gly	Val	Ala	Arg	Ala	Leu	Ala	His	Gly	Val	Arg	Ala	Val	Glu	Asp
145					150					155					160

Gly Ile Asn Tyr Ala Thr 165

- (2) INFORMATION FOR SEQ ID NO: 165:
 - (i) SEQUENCE CHARACTERISTICS:
 - (A) LENGTH: 499 base pairs
 - (B) TYPE: nucleic acid
 - (C) STRANDEDNESS: single
 (D) TOPOLOGY: linear
 - (ii) MOLECULE TYPE: DNA (genomic)
 - (iii) HYPOTHETICAL: NO
 - (iii) ANTI-SENSE: NO
 - (xi) SEQUENCE DESCRIPTION: SEQ ID NO: 165:

ATGAGCACGA ATCCTAAACC TCAAAGAAAA ACCAAACGTA ACACCAACCG CCGCCCTATG 60 GACGTTAAGT TCCCAGGCGG TGGTCAGATC GTTGGCGGAG TTTACTTGTT GCCGCGCAGG 120 GGCCCCAGGT TGGGTGTGCG CGCGACTCGG AAGACTTCGG AGCGGTCGCA ACCTCGTGGG 180 AGGCGCCAAC CTATCCCCAA GGCGCGCCGA ACCGAGGGCA GATCCTGGGC GCAGCCCGGG 240 TATCCTTGGC CCCTTTACGG CAATGAGGGC TGTGGGTGGG CAGGGTGGCT CCTGTCCCCT 300 CGCGGNTCTC GGNCGTCTTG GGGCCCCAAT GATCCCCGGN GGAGATCCCG CAACTTGGGT 360 AAGGTCATCG ATACCCTAAC ATGCGGCTTC GCCGACCTCA TGGGATACAT CCCGCTTGTA 420 GGCGCCCCCG TGGGTGGCGT CGCCAGGGCC CTGGCACATG GTGTTAGGGC TGTGGAAGAC 480 GGGATCAATT ATGCAACAG 499

- (2) INFORMATION FOR SEQ ID NO: 166:
 - (i) SEQUENCE CHARACTERISTICS:
 - (A) LENGTH: 126 amino acids
 - (B) TYPE: amino acid
 - (C) STRANDEDNESS: single
 (D) TOPOLOGY: linear

 - (ii) MOLECULE TYPE: protein
 - (xi) SEQUENCE DESCRIPTION: SEQ ID NO: 166:

Met Ser Thr Asn Pro Lys Pro Gln Arg Lys Thr Lys Arg Asn Thr Asn

	1				5					10					15		
	Arg	Arg	Pro	Met 20	Asp	Val	Lys	Phe	Pro 25	Gly	Gly	Gly	Gln	Ile 30	Val	Gly	
	Gly	Val	Tyr 35	Leu	Leu	Pro	Arg	Arg 40	Gly	Pro	Arg	Leu	Gly 45	Val	Arg	Ala	
	Thr	Arg 50	Lys	Thr	Ser	Glu	Arg 55	Ser	Gln	Pro	Arg	Gly 60	Arg	Arg	Gln	Pro	
	Ile 65	Pro	Lys	Ala	Arg	Arg 70	Thr	Glu	Gly	Arg	Ser 75	Trp	Ala	Gln	Pro	Gly 80	
	Tyr	Pro	Trp	Pro	Leu 85	Tyr	Gly	Asn	Glu	Gly 90	Cys	Gly	Trp	Ala	Gly 95	Trp	
	Leu	Leu	Ser	Pro 100	Arg	Xaa	Ser	Arg	Xaa 105	Ser	Trp	Gly	Pro	Asn 110	Asp	Pro	
	Arg	Xaa	Arg 115	Ser	Arg	Asn	Leu	Gly 120	Lys	Val	Ile	Asp	Thr 125	Leu			
(2)	INFO	RMAT:	ON I	OR S	BEQ :	ID NO	: 1	57:									
	(i)	(B)	LEN TYI	GTH: PE: 1 RANDE	57: nucle	reris 9 bas eic a es: s lines	se pa acid sing:	airs									
	(ii)	MOLI	CUL	TYI	PE: 0	DNA											
	(iii)	HYPO	THE	CICAL	. NO	0											
	(iii)	ANT	-SEN	ISE :	NO												
	(ix)	(A)	NAM	E/KE		CDS L57	79										
	(ix)	(A)	NAM	E/K		mat_ <u>r</u> 157		ide									
	(xi)	SEQ	JENCI	DES	CRI	PTION	1: SI	SQ II	NO.	: 16	7:						
	TGC (48
	GTG (96
GAA	GAC (agg 2	ATC Z	AAT 1	rat (3CA 2	ACA (3GG 2	AAC (TT (ecc o	GT :	rgc :	rec :	TTT		144

Glu	Asp	Gly 35	Ile	Asn	Tyr	Ala	Thr 40	Gly	Asn	Leu	Pro	Gly 45	Сув	Ser	Phe	
								TCG Ser							TCG Ser	192
								GGC Gly								240
								GAG Glu								288
								AGG Arg 105								336
								GCG Ala								384
								GAC Asp								432
								gac Asp								480
								CCG Pro								528
GAC Asp								GGC Gly 185								576
GCA Ala																579

- (2) INFORMATION FOR SEQ ID NO: 168:
 - (i) SEQUENCE CHARACTERISTICS:
 - (A) LENGTH: 193 amino acids
 - (B) TYPE: amino acid (D) TOPOLOGY: linear
 - (ii) MOLECULE TYPE: protein
 - (xi) SEQUENCE DESCRIPTION: SEQ ID NO: 168:

Thr Cys Gly Phe Ala Asp Leu Met Gly Tyr Ile Pro Leu Val Gly Ala

Pro Val Gly Val Ala Arg Ala Leu Ala His Gly Val Arg Ala Val $20 \hspace{1.5cm} \textbf{25} \hspace{1.5cm} \textbf{30}$

Glu Asp Gly Ile Asn Tyr Ala Thr Gly Asn Leu Pro Gly Cys Ser Phe \$35\$

Ser Ile Phe Leu Leu Ala Leu Leu Ser Cys Leu Thr Val Pro Thr Ser 50 55 60

Ala Val Asn Tyr Arg Asn Ala Ser Gly Ile Tyr His Ile Thr Asn Asp 65 70 75 80

Cys Pro Asn Ala Ser Ile Val Tyr Glu Thr Glu Asn His Ile Leu His 85 90 95

Leu Pro Gly Cys Val Pro Cys Val Arg Thr Gly Asn Gln Ser Arg Cys
100 105 110

Trp Val Ala Leu Thr Pro Thr Val Ala Ser Pro Tyr Ala Gly Ala Pro 115 120 125

Leu Glu Pro Leu Arg Arg His Val Asp Leu Met Val Gly Ala Ala Thr 130 140

Met Cys Ser Ala Leu Tyr Ile Gly Asp Leu Cys Gly Gly Leu Phe Leu 145 150 155 160

Val Gly Gln Met Phe Thr Phe Gln Pro Arg Arg His Trp Thr Thr Gln 165 170 175

Asp Cys Asn Cys Ser Ile Tyr Thr Gly His Ile Thr Gly His Arg Met 180 $$185\ \ \, 190\ \ \,$

- (2) INFORMATION FOR SEQ ID NO: 169:
 - (i) SEQUENCE CHARACTERISTICS:
 - (A) LENGTH: 579 base pairs
 - (B) TYPE: nucleic acid
 - (C) STRANDEDNESS: single (D) TOPOLOGY: linear
 - (ii) MOLECULE TYPE: cDNA
 - (iii) HYPOTHETICAL: NO

 - (iii) ANTI-SENSE: NO
 - (ix) FEATURE:
 - (A) NAME/KEY: CDS
 - (B) LOCATION: 1..579
 - (ix) FEATURE:
 - (A) NAME/KEY: mat peptide
 - (B) LOCATION: 1..576

(xi)	SECUENCE	DESCRIPTION:	SEO	ID	NO:	169:	

	TGC Cys		GCC Ala 5							48
	GTG Val									96
	GAC Asp									144
	ATC Ile 50								TCG Ser	192
	GTT Val									240
	CCG Pro									288
	CCA Pro									336
	GTG Val									384
	GAG Glu 130									432
	TGC Cys									480
	GGC Gly									528
GAC Asp	TGT Cys									576
GCT Ala										579

(2) INFORMATION FOR SEQ ID NO: 170:

- (i) SEQUENCE CHARACTERISTICS:
 - (A) LENGTH: 193 amino acids
 - (B) TYPE: amino acid (D) TOPOLOGY: linear
- (ii) MOLECULE TYPE: protein
- (xi) SEQUENCE DESCRIPTION: SEQ ID NO: 170:

Thr Cys Gly Phe Ala Asp Leu Met Gly Tyr Ile Pro Leu Val Gly Ala 10

Pro Val Gly Gly Val Ala Arg Ala Leu Ala His Gly Val Arg Ala Val 25

Glu Asp Gly Ile Asn Tyr Ala Thr Gly Asn Leu Pro Gly Cys Ser Phe

Ser Ile Phe Leu Leu Ala Leu Leu Ser Cys Leu Thr Val Pro Ala Ser 55

Gly Val Asn Tyr Arg Asn Ala Ser Gly Val Tyr His Ile Thr Asn Asp

Cys Pro Asn Ala Ser Ile Val Tyr Glu Thr Asp Asn His Ile Leu His

Leu Pro Gly Cys Val Pro Cys Val Lys Thr Gly Asn Gln Ser Arg Cys

Trp Val Ala Leu Thr Pro Thr Val Ala Ser Pro Tyr Val Gly Ala Pro

Leu Glu Pro Leu Arg Arg His Val Asp Leu Met Val Gly Ala Ala Thr

Val Cys Ser Ala Leu Tyr Val Gly Asp Leu Cys Gly Gly Leu Phe Leu 155

Val Gly Gln Met Phe Thr Phe Gln Pro Arg Arg His Trp Thr Thr Gln 165 170

Asp Cys Asn Cys Ser Ile Tyr Ala Gly His Ile Thr Gly His Arg Met

- (2) INFORMATION FOR SEO ID NO: 171:
 - (i) SEQUENCE CHARACTERISTICS:
 - (A) LENGTH: 579 base pairs (B) TYPE: nucleic acid

 - (C) STRANDEDNESS: single (D) TOPOLOGY: linear
 - (ii) MOLECULE TYPE: cDNA

- (iii) HYPOTHETICAL: NO
- (iii) ANTI-SENSE: NO
- (ix) FEATURE:
 - (A) NAME/KEY: CDS
 - (B) LOCATION: 1..579
- (ix) FEATURE:
 - (A) NAME/KEY: mat peptide
 - (B) LOCATION: 1..576
- (xi) SEQUENCE DESCRIPTION: SEQ ID NO: 171:

ACA	TGC	GGC	TTC	GCC	GAC	CTC	ATG	GGA	TAC	ATC	CCG	CTT	GTG	GGC	GCC	48
Thr	Сув	Gly	Phe	Ala	Asp	Leu	Met	Gly	Tyr	Ile	Pro	Leu	Val	Gly	Ala	
1				5					10					15		

CCT GTT GGT GGC GTC GCC AGA GCC CTT GGG CAC GGC GTC AGG GCT GTG
Pro Val Gly Val Ala Arg Ala Leu Ala His Gly Val Arg Ala Val
20 25 30

GAA GAC GGG ATT AAC TAT GCA ACA GGG AAC CTT CCT GGT TGC TCT TT GLU Asp Gly Ile Asn Tyr Ala Thr Gly Asn Leu Pro Gly Cys Ser Phe 45 45

TCT ATC TTC CTT CTG GCA CTT CTC TCG TGC CTG ACT GTC CCC GCC TCG Ser ILe Phe Leu Leu Ala Leu Leu Ser Cys Leu Thr Val Pro Ala Ser 50 60 60

GCT GTG CAT TAT CAC AAC ACC TCG GGC ATC TAC CAC CTC ACC AAT GAC
Ala Val His Tyr His Asn Thr Ser Gly Ile Tyr His Leu Thr Asn Asp
65 70 80

TGC CCT AAC TCT AGC ATA GTC TTT GAG GCA GTC CAT CAC ATC TTG CAC

Cys Pro Asn Ser Ser Ile Val Phe Glu Ala Val His His Ile Leu His

85 90 95

CTT CCA GGA TGC GTC CCT TGT GTA AGA ACT GGG AAC CAG TCT CGG TGC
Leu Pro Gly Cys Val Pro Cys Val Arg Thr Gly Asn Gln Ser Arg Cys
100 100 110 110

TGG GTA GCC TTG ACC CCC ACG CTG GCC GCG CCA TAC CTT GGC GCT CCA
Trp Val Ala Leu Thr Pro Thr Leu Ala Ala Pro Tyr Leu Gly Ala Pro
115 120 125

CTC GAG TCC ATG CGG CGT CAC GTG GAT TTG ATG GTG GGC ACT GCT ACA
Leu Glu Ser Met Arg Arg His Val Asp Leu Met Val Gly Thr Ala Thr
130
135
140

TTG TGC TCA GCA CTC TAC GTT GGG GAC CTG TGC GGG GGC ATA TTC CTA 480 Leu Cys Ser Ala Leu Tyr Val Gly Asp Leu Cys Gly Gly Ile Phe Leu 150 155 156 166

GCG GGC CAG ATG TTC ACC TTC CGG CCC CGC CTC CAT TGG ACC ACC CAG
Ala Gly Gln Met Phe Thr Phe Arg Pro Arg Leu His Trp Thr Thr Gln
165
170
175

GAG TGC AAT TGT TGC ACC TAT CGG GGC CAC ATC AGG GGT CAT AGA ATG Glu Cys Asn Cys Ser Thr Tyr Pro Gly His Ile Thr Gly His Arg Met 180 576

GCG Ala 579

- (2) INFORMATION FOR SEQ ID NO: 172:
 - (i) SEQUENCE CHARACTERISTICS:(A) LENGTH: 193 amino acids
 - (B) TYPE: amino acid
 - (D) TOPOLOGY: linear
 - (ii) MOLECULE TYPE: protein
 - (xi) SEQUENCE DESCRIPTION: SEQ ID NO: 172:

Thr Cys Gly Phe Ala Asp Leu Met Gly Tyr Ile Pro Leu Val Gly Ala

Pro Val Gly Gly Val Ala Arg Ala Leu Ala His Gly Val Arg Ala Val 20 25 30

Glu Asp Gly Ile Asn Tyr Ala Thr Gly Asn Leu Pro Gly Cys Ser Phe 35 40 45

Ser Ile Phe Leu Leu Ala Leu Leu Ser Cys Leu Thr Val Pro Ala Ser 50 55 60

Ala Val His Tyr His Asn Thr Ser Gly Ile Tyr His Leu Thr Asn Asp 65 70 75 80

Cys Pro Asn Ser Ser Ile Val Phe Glu Ala Val His His Ile Leu His 85 90 95

Leu Pro Gly Cys Val Pro Cys Val Arg Thr Gly Asn Gln Ser Arg Cys 100 105 110

Trp Val Ala Leu Thr Pro Thr Leu Ala Ala Pro Tyr Leu Gly Ala Pro 115 120 125

Leu Glu Ser Met Arg Arg His Val Asp Leu Met Val Gly Thr Ala Thr 130 135 140

Leu Cys Ser Ala Leu Tyr Val Gly Asp Leu Cys Gly Gly Ile Phe Leu 145 150 155 160

Ala Gly Gln Met Phe Thr Phe Arg Pro Arg Leu His Trp Thr Thr Gln 165 170 175

Glu Cys Asn Cys Ser Thr Tyr Pro Gly His Ile Thr Gly His Arg Met 180 185 190

(2)	INF	ORMA!	TION	FOR	SEQ	ID I	(O)	173:						
	(i)	(1		engti YPE : IRANI	i: 57	79 ba leic ESS:	ase p acid	pair:	s					
	(ii)	MOI	ECUI	LE T	PE:	CDN	A							
	(iii)	HY	отні	STIC	L: 1	10								
	(iii)	AN.	ri-si	ense	: NO									
	(ix)		ATURI A) NI B) Lo	AME/I			579							
	(ix)		ATURI A) Ni B) Lo	AME/I				ide						
	(xi)	SEÇ	QUEN	CE DI	SCR	PTI	on: s	SEQ :	ID N): 1:	73:			
	TGC Cys													48
	GTG Val													96
	GAC Asp											Cys		144
	ATC Ile 50													192
	GTG Val													240
	CCT Pro													288
	CCA Pro													336
	ATA Ile												CCA Pro	384

125

CTT GAG TCC ATG CGA CGT CAT GTG GAT TTG ATG GTA GGC ACT GCC ACA 432 Leu Glu Ser Met Arg Arg His Val Asp Leu Met Val Gly Thr Ala Thr

TTG TGC TCC GCA CTC TAC ATT GGA GAT CTG TGC GGA GGC ATA TTT CTA 480 Leu Cys Ser Ala Leu Tyr Ile Gly Asp Leu Cys Gly Gly Ile Phe Leu 150

GTG GGC CAG ATG TTC AAC TTC AGG CCC CGC CTG CAC TGG ACC ACC CAG 528 Val Gly Gln Met Phe Asn Phe Arg Pro Arg Leu His Trp Thr Thr Gln

GAG TGC AAT TGT TCC ATC TAT CCA GGC CAC ATC ACG GGT CAC AGA ATG 576 Glu Cys Asn Cys Ser Ile Tyr Pro Gly His Ile Thr Gly His Arg Met 180

GCG 579 Ala

- (2) INFORMATION FOR SEQ ID NO: 174:
 - (i) SEQUENCE CHARACTERISTICS:
 - (A) LENGTH: 193 amino acids
 - (B) TYPE: amino acid (D) TOPOLOGY: linear
 - (ii) MOLECULE TYPE: protein
 - (xi) SEQUENCE DESCRIPTION: SEQ ID NO: 174:

Thr Cys Gly Ser Ala Asp Leu Met Gly Tyr Ile Pro Leu Val Gly Ala 1 10

Pro Val Gly Gly Val Ala Arg Ala Leu Ala His Gly Val Arg Ala Val

Glu Asp Gly Ile Asn Tyr Ala Thr Gly Asn Leu Pro Gly Cys Ser Phe

Ser Ile Phe Leu Leu Ala Leu Leu Ser Cys Leu Thr Val Pro Ala Ser

Ala Val His Tyr His Asn Thr Ser Gly Ile Tyr His Ile Thr Asn Asp

Cys Pro Asn Ser Ser Ile Val Phe Glu Ala Glu His His Ile Leu His - 85

Leu Pro Gly Cys Val Pro Cys Val Arg Thr Gly Asn Gln Ser Arg Cys

Trp Ile Ala Leu Thr Pro Thr Leu Ala Ala Pro His Ile Gly Ala Pro 120

224	
Leu Glu Ser Met Arg Arg His Val Asp Leu Met Val Gly Thr Al 130 135	la Thr
Leu Cys Ser Ala Leu Tyr Ile Gly Asp Leu Cys Gly Gly Ile Pi 145 150 155	he Leu . 160
Val Gly Gln Met Phe Asn Phe Arg Pro Arg Leu His Trp Thr Th 165 170 17	
Glu Cys Asn Cys Ser Ile Tyr Pro Gly His Ile Thr Gly His Ar 180 185	rg Met
Ala	
(2) INFORMATION FOR SEQ ID NO: 175:	
(i) SEQUENCE CHARACTERISTICS: (A) LENGTH: 579 base pairs (B) TYPE: nucleic acid (C) STRANDEDNESS: single (D) TOPOLOGY: linear	
(ii) MOLECULE TYPE: cDNA	
(iii) HYPOTHETICAL: NO	
(iii) ANTI-SENSE: NO	
(ix) FEATURE: (A) NAME/KEY: CDS (B) LOCATION: 1579	
(ix) FEATURE: (A) NAME/KEY: mat_peptide (B) LOCATION: 1576	
(xi) SEQUENCE DESCRIPTION: SEQ ID NO: 175:	
acg toc GGC TTT GCC GAC CTC ATG GGA TAC ATC CCG CTC GTG GG Thr Cys Gly Phe Ala Asp Leu Met Gly Tyr Ile Pro Leu Val Gl 1 5 10 1	
CCT GTG GGT GGC GTC GCC AGG GCC TTG GCA CAT GGT GTC AGG GC Pro Val Gly Gly Val Ala Arg Ala Leu Ala His Gly Val Arg Al	
20 25 30	.a vai
GAG GAC GGG ATT AAC TAT GCA ACA GGG AAT CTT CCC GGT TGC TC	
Glu Asp Gly Ile Asn Tyr Ala Thr Gly Asn Leu Pro Gly Cys Se 35 40 45	er Phe
TCT ATC TTC CTT CTA GCA CTT CTC TCG TGC TTG ACT GTC CCG GC Ser Ile Phe Leu Leu Ala Leu Leu-Ser Cys Leu Thr Val Pro Al 50° 60	
GCG CAG CAC TAC CGG AAC ATC TCG GGC ATT TAT CAC GTC ACC AA	
Ala Gln His Tyr Arg Asn Ile Ser Gly Ile Tyr His Val Thr As	n Asp

WO 94	/2560)1												PCT/	EP94/0	1323
								22	25							
65					70					75				80		
														CAT His		288
			TGT Cys 100											TGC Cys		336
			TTA Leu											CCG Pro		384
			ATG Met													432
			GCC Ala													480
			ATG Met													528
			TGC Cys 180													576
GCT Ala																579
(2)		(i) S (Z (E	FION SEQUE A) LE B) TO	ence engti pe :	CHAI I: 19	RACTE 93 an	RIST nino sid	rics:								
			JECUI QUENC			-		SEQ 1	D NO): 17	76:					
		_								_		_	_			

SUBSTITUTE SHEET (RULE 26)

Thr Cys Gly Phe Ala Asp Leu Met Gly Tyr Ile Pro Leu Val Gly Ala 1 10 15

Prc Val Gly Cly Val Ala Arg Ala Leu Ala His Gly Val Arg Ala Val
25
Glu Asp Gly Ile Asn Tyr Ala Thr Gly Asn Leu Pro Gly Cys Ser Phe
35
40
Ser Ile Phe Leu Leu Ala Leu Leu Ser Cys Leu Thr Val Pro Ala Ser

55

. 50

Ala Gln His Tyr Arg Asn Ile Ser Gly Ile Tyr His Val Thr Ash Asp 65 70 75 80

Cys Pro Asn Ser Ser Ile Val Tyr Glu Ala Asp His His Ile Met His
85 90 95

Leu Pro Gly Cys Val Pro Cys Val Arg Thr Gly Asn Thr Ser Arg Cys
100 105 110

Trp Val Pro Leu Thr Pro Thr Val Ala Ala Pro Tyr Val Gly Ala Pro

Leu Glu Ser Met Arg Arg His Val Asp Leu Met Val Gly Ala Ala Thr 130 135 140

Val Cys Ser Ala Leu Tyr Ile Gly Asp Leu Cys Gly Gly Val Phe Leu 145 150 155 160

Val Gly Gln Met Phe Thr Phe Arg Pro Arg Arg His Trp Thr Thr Gln 165 170 175

Asp Cys Asn Cys Ser Ile Tyr Asp Gly His Ile Thr Gly His Arg Met 180 \$180\$

- (2) INFORMATION FOR SEO ID NO: 177:
 - (i) SEQUENCE CHARACTERISTICS:
 - (A) LENGTH: 579 base pairs
 - (B) TYPE: nucleic acid
 - (C) STRANDEDNESS: single (D) TOPOLOGY: linear
 - (ii) MOLECULE TYPE: cDNA
 - (iii) HYPOTHETICAL: NO
 - (iii) ANTI-SENSE: NO
 - (ix) FEATURE:
 - (A) NAME/KEY: CDS
 - (B) LOCATION: 1..579
 - (ix) FEATURE:
 - (A) NAME/KEY: mat_peptide
 - (B) LOCATION: 1..576
 - (xi) SEQUENCE DESCRIPTION: SEQ ID NO: 177:
- ACG TGC GGG TTC GCC GAC CTC ATG GGA TAC ATC CCG CTC GTG GGC GCT Thr Cys Gly Phe Ala Asp Leu Met-Gly Tyr ILe Pro Leu Val Gly Ala 1 1 10 15
- CCA GTA GGA GGC GTC GCC AGA GCC TTG GCG CAT GGC GTC AGG GCT GTG
 Pro Val Gly Gly Val Ala Arg Ala Leu Ala His Gly Val Arg Ala Val

		20			25			30		
									TTT Phe	144
				CTC Leu						192
				TCG Ser						240
				TAT Tyr						288
				GTA Val						336
				GTA Val 120						384
				GTG Val						432
TTA Leu 145				GGA Gly						480
GCA Ala										528
GAT Asp										576

579

(2) INFORMATION FOR SEQ ID NO: 178:

GCC

- (i) SEQUENCE CHARACTERISTICS:
 - (A) LENGTH: 193 amino acids
 - (B) TYPE: amino acid
 - (D) TOPOLOGY: linear
- (ii) MOLECULE TYPE: protein
- (xi) SEQUENCE DESCRIPTION: SEQ ID NO: 178:

Thr Cys Gly Phe Ala Asp Leu Met Gly Tyr Ile Pro Leu Val Gly Ala
1 10 15
Pro Val Gly Gly Val Ala Arg Ala Leu Ala His Gly Val Arg Ala Val

Glu Asp Gly Ile Asn Tyr Ala Thr Gly Asn Leu Pro Gly Cys Ser Phe

Ser Ile Phe Leu Leu Val Leu Leu Ser Arg Leu Thr Val Pro Ala Ser

50 55 60

Ala Gln His Tyr Arg Asn Ala Ser Gly Ile Tyr His Val Thr Asn Asp 65 70 75 80

Cys Pro Asn Ser Ser Ile Val Tyr Glu Ala Asp His His Ile Met His

85 90 95

Leu Pro Gly Cys Val Pro Cys Val Arg Thr Gly Asn Val Ser Arg Cys
100 105 110

Trp Ile Pro Leu Thr Pro Thr Val Ala Val Pro Tyr Leu Gly Ala Pro 115 120 125

Leu Thr Ser Val Arg Gln His Val Asp Leu Met Val Gly Ala Ala Thr 130 135 140

Leu Cys Ser Ala Leu Tyr Ile Gly Asp His Cys Gly Gly Val Phe Leu 145 150 155 160

Ala Gly Gln Met Val Ser Phe Gln Pro Arg Arg His Trp Thr Thr Gln 165 170 175

Asp Cys Asn Cys Ser Ile Tyr Val Gly His Ile Thr Gly His Arg Met 180 185 190

- (2) INFORMATION FOR SEQ ID NO: 179:
 - (i) SEQUENCE CHARACTERISTICS:
 - (A) LENGTH: 579 base pairs
 - (B) TYPE: nucleic acid
 - (C) STRANDEDNESS: single
 (D) TOPOLOGY: linear

 - (ii) MOLECULE TYPE: CDNA
 - (iii) HYPOTHETICAL: NO
 - (iii) ANTI-SENSE: NO
 - (ix) FEATURE:
 - (A) NAME/KEY: CDS
 - (B) LOCATION: 1..579

	DESCRIPTION:		

ACCTGCGGCT	TCGCCGACCT	CATGGGATAC	ATCCCGCTCG	TAGGCGCCCC	CGTGGGAGGC	60
GTCGCCAGAR	CTCTGGCGCA	TGGCGTCAGG	GCTCTGGAAG	ACGGGATCAA	TTATGCAACA	120
GGGAATCTTC	CTGGTTGCTC	TTTCTCTATC	TCCCTTCTTG	AACTTCTCTC	GTGCCTGACT	180
GTTCCCGCCT	CAGCCATCCA	CTATCGCAAT	GCTTCGGACG	GTTATTATAT	CACCAATGAT	240
TGCCCGAACT	CTAGCATAGT	GTATGAAGCC	GAGAACCACA	TCTTGCACCT	TCCGGGGTGT	300
ATACCCTGTG	TGAAGACCGG	GAATCAGTCG	CGGTGCTGGG	TGGCTCTCAC	CCCCACGCTG	360
GCGGCCCCAC	ACCTACGTGC	TCCGCTTTCG	TCCTTACGGG	CGCATGTGGA	CCTAATGGTG	420
GGGGCCGCCA	CGGCATGCTC	CGCTTTTTAC	ATTGGAGATC	TGTGCGGGGG	TGTGTTTTTG	480
GCGGGCCAAC	TGTTCACTAT	CCGGCCACGC	ATTCATGAAA	CCACTCAGGA	CTGCAATTGC	540
TCCATCTACT	CAGGGCACAT	CACGGGTNNN	NNNNNNNN			579

- (2) INFORMATION FOR SEQ ID NO: 180:
 - (i) SEQUENCE CHARACTERISTICS:
 - (A) LENGTH: 193 amino acids
 - (B) TYPE: amino acid
 - (C) STRANDEDNESS: single
 (D) TOPOLOGY: linear
 - (ii) MOLECULE TYPE: protein
 - (xi) SEQUENCE DESCRIPTION: SEQ ID NO: 180: Thr Cys Gly Phe Ala Asp Leu Met Gly Tyr Ile Pro Leu Val Gly Ala
 - 1 5 10 15
 - Pro Val Gly Val Ala Arg Xaa Leu Ala His Gly Val Arg Ala Leu 20 25 30
 - Glu Asp Gly Ile Asn Tyr Ala Thr Gly Asn Leu Pro Gly Cys Ser Phe $35 \hspace{1cm} 40 \hspace{1cm} 45$
 - Ser Ile Ser Leu Leu Glu Leu Leu Ser Cys Leu Thr Val Pro Ala Ser 50 55 60
 - Ala Ile His Tyr Arg Asn Ala Ser Asp Gly Tyr Tyr Ile Thr Asn Asp 65 75 80
 - Cys Pro Asn Ser Ser Ile Val Tyr Glu Ala Glu Asn His Ile Leu His 85 90 95
 - Leu Pro Gly Cys Ile Pro Cys Val Lys Thr Gly Asn Gln Ser Arg Cys

300

480

Leu	Leu Ser Ser Leu Arg Ala His Val Asp Leu Met Val Gly Ala Ala Thr 130 Ala Cys Ser Ala Phe Tyr Ile Gly Asp Leu Cys Gly Gly Val Phe Leu 145 150 Ala Gly Gln Leu Phe Thr Ile Arg Pro Arg Ile His Glu Thr Thr Gln 165 Asp Cys Asn Cys Ser Ile Tyr Ser Gly His Ile Thr Gly Xaa Xaa Xaa 180 Xaa															
	Сув	Ser	Ala	Phe		Ile	Gly	Asp	Leu		Gly	Gly	Val	Phe		
Ala	Gly	Gln	Leu		Thr	Ile	Arg	Pro		Ile	His	Glu	Thr		Gln	
Asp	Cys	Asn		Ser	Ile	Tyr	Ser		His	Ile	Thr	Gly		Xaa	Xaa	
Xaa																
(2) INFO	·															
(2) INFORMATION FOR SEQ ID NO: 181: (i) SEQUENCE CHARACTERISTICS: (i) LENGTH: 579 base pairs (ii) TYPE: nucleic acid (iii) STRANDENDESS: single (iii) TOPOLOGY: linear																
(ii)	MOLE	CULE	TY	PE: 0	:DNA											
(iii)	HYPO	THET	ricai	.: NO)											
(iii)	ANTI	-SEN	ISE:	NO												
(ix)	(A)	NAN	: ME/KE CATIO			78										
(xi)	SEQU	JENCE	E DES	CRII	TIO	1: SI	EQ II	NO:	181	.:						
GCGTGCGG	T TO	GCCG	ATCI	CAT	rgggz	TAC	ATC	CCGC	rCG 7	AGGG	cgccc	ec co	TGGG	TGGC	;	60

GTCGCCAGAG CCCTGGCGCA CGGTGTTAGG GCTGTGGAGG ACGGGATTAA CTACGCAACA GGGAATCTTC CTGGTTGCTC TTTCTCTATC TNCCTTCTGG CACTTCTCTC GTGCCTGACT GTCCCGGCCT CGGCTCAGCA CTACCGGAAT GTCTCGGGCA TCTACCACGT CACCAATGAT

TGCCCGAATT CCAGCATAGT GTATGAAGCC GATCACCACA TCATGCACTT ACCAGGGTGC

ATACCCTGCG TGAGGACCGG GAACGTTTCG CGCTGCTGGG TATCTCTGAC ACCTACTGTG GCTGCTCCCT ACCTCGGGGC TCCGCTTACG TCGCTACGGC GGCATGTGGA TTTGATGGTG GGTGCAGCCA CCCTTTGCTC TGCCCTCTAC GTCGGAGACC TCTGTGGAGG TGTCTTCCTA

GTGG	GACA	GA T	GTTC	ACCT	T CC	AGCC	GCGC	CGC	CACT	GGA	CCAC	TCAG	GA C	TGCA	ACTG	c	540
TCCA	TTTA	CG T	CGGC	CACA	T CA	CAGG	CCAC	AGA	ATGG	CT							579
(2)	INFO	SEQI (A (B	UENC LE TY	FOR : E CHL NGTH PE: : RAND	ARAC : 19 amin	TERI: 3 am: 0 ac: SS:	STIC ino id sing	S: acid	s								
	(ii)	MOL	BCOT	E TY	PE:]	prot	ein										
	(xi)	SEQ	JENC	E DE:	SCRI	PTIO	N: S	BQ II	D NO	: 18	2:						
	Ala 1	Cys	Gly	Phe	Ala 5	Asp	Leu	Met	Gly	Tyr 10	Ile	Pro	Leu	Val	Gly 15	Ala	
	Pro	Val	Gly	Gly 20	Val	Ala	Arg	Ala	Leu 25	Ala	His	Gly	Val	Arg 30	Ala	Val	
	Glu	Asp	Gly 35	Ile	Asn	Tyr	Ala	Thr 40	Gly	Asn	Leu	Pro	Gly 45	Cys	Ser	Phe	
	Ser	Ile 50	Xaa	Leu	Leu	Ala	Leu 55	Leu	Ser	Cys	Leu	Thr 60	Val	Pro	Ala	Ser	
	Ala 65	Gln	His	Tyr	Arg	Asn 70	Val	Ser	Gly	Ile	Tyr 75	His	Val	Thr	Asn	Asp 80	
	Сув	Pro	Asn	Ser	Ser 85	Ile	Val	Tyr	Glu	Ala 90	Asp	His	His	Ile	Met 95	His	
	Leu	Pro	Gly	Cys 100	Ile	Pro	Сув	Val	Arg 105	Thr	Gly	Asn	Val	Ser 110	Arg	Cys	
	Trp	Val	Ser 115	Leu	Thr	Pro	Thr	Val 120	Ala	Ala	Pro	Tyr	Leu 125	Gly	Ala	Pro	
	Leu	Thr 130	Ser	Leu	Arg	Arg	His 135	Val	Asp	Leu	Met	Val 140	Gly	Ala	Ala	Thr	
	Leu 145	Cys	Ser	Ala	Leu	Tyr 150	Val	Gly	qaA	Leu	Cys 155	Gly	Gly	Val	Phe	Leu 160	
	Val	Gly	Gln	Met	Phe 165	Thr	Phe	Gln	Pro	Arg 170	Arg	His	Trp	Thr	Thr 175	Gln	
	Asp	Сув	Asn	Cys 180	Ser	Ile	туг	Val	Gly 185	His	Ile	Thr	Gly	His 190	Arg	Met	

(A) TURANUETAN DAD ARA TO NO. 102	
(2) INFORMATION FOR SEQ ID NO: 183:	
(i) SEQUENCE CHARACTERISTICS: (A) LENOTH: 579 base pairs (B) TYPE: nucleic acid (C) STRANDEINESS: single (D) TOFOLOGY: linear	
(ii) MOLECULE TYPE: cDNA	
(iii) HYPOTHETICAL: NO	
(iii) ANTI-SENSE: NO	
(ix) FEATURE:	
(A) NAME/KEY: CDS	
(B) LOCATION: 1579	
(ix) FEATURE:	
(A) NAME/KEY: mat_peptide (B) LOCATION: 1579	
(B) EOCATION: 1579	
V	
(xi) SEQUENCE DESCRIPTION: SEQ ID NO: 183:	
ACC TGC GGC TTT GCC GAC CTC ATG GGA TAC ATC CCG CTC GTA GGC GCC	4
Thr Cys Gly Phe Ala Asp Leu Met Gly Tyr Ile Pro Leu Val Gly Ala	
1 5 10 15	
CCT GTG GGT GGC GTC GCC AGG GCC CTA GAA CAC GGT GTT AGG GCT GTG	9
Pro Val Gly Gly Val Ala Arg Ala Leu Glu His Gly Val Arg Ala Val 20 25 30	
GAG GAC GGT ATT AAT TAT GCA ACA GGG AAT CTC CCC GGT TGC TCT TTT Glu Asp Gly Ile Asn Tyr Ala Thr Gly Asn Leu Pro Gly Cys Ser Phe	14
35 40 45	
TCT ATC TCC CTC TTG GCA CTT CTT TCG TGC CTG ACT GTT CCC ACC TCA	19
Ser Ile Ser Leu Leu Ala Leu Leu Ser Cys Leu Thr Val Pro Thr Ser	10
50 55 60	
GCC GTC AAC TAT CGC AAC GCC TCG GGC GTC TAT CAT ATC ACC AAT GAC	24
Ala Val Asn Tyr Arg Asn Ala Ser Gly Val Tyr His Ile Thr Asn Asp	
65 70 75 80	
TGC CCG AAT TCG AGC ATA GTG TAC GAG GCT GAC TAC CAC ATC CTA CAC	28
Cys Pro Asn Ser Ser Ile Val Tyr Glu Ala Asp Tyr His Ile Leu His	
85 90 95	
CTC CCT GGG TGC TTA CCC TGC GTG AGG GTT GGG AAT CAG TCA CGC TGC	33
Leu Pro Gly Cys Leu Pro Cys Val Arg Val Gly Asn Gln Ser Arg Cys	
700 700 770	
TGG GTG GCC CTT ACT CCC ACC GTG GCG GCG CCT TAC GTT GGT GCT CCG	38
Trp Val Ala Leu Thr Pro Thr Val Ala Ala Pro Tyr Val Gly Ala Pro	

115 120 125

CTA GAA TCC CTC CGG AGT CAT GTG GAT CTG ATG GTA GGT GCT ACT
432
Leu Glu Ser Leu Arg Ser His Val Asp Leu Met Val Gly Ala Ala Thr
130
135
140

GTT GGT CAG ATG TTT TCT TTC CAG CCG CGA CGC CAC TGG ACC CAG CAG Val Gly Gln Met Phe Ser Phe Gln Pro Arg Arg His Trp Thr Thr Gln

165 170 175
GAC TGC AAT TGT TCT ATC TAC GGC GGG CAC GTT ACG GGC CAC AGG ATG 576
Asp Cys Asn Cys Ser Ile Tyr Ala Gly His Val Thr Gly His Arg Met
180 180

GCA 579 Ala

- (2) INFORMATION FOR SEQ ID NO: 184:
 - (i) SEQUENCE CHARACTERISTICS:
 - (A) LENGTH: 193 amino acids
 - (B) TYPE: amino acid (D) TOPOLOGY: linear
 - (ii) MOLECULE TYPE: protein
 - (xi) SEQUENCE DESCRIPTION: SEQ ID NO: 184:

Thr Cys Gly Phe Ala Asp Leu Met Gly Tyr Ile Pro Leu Val Gly Ala 1 5 10 15

Pro Val Gly Gly Val Ala Arg Ala Leu Ala His Gly Val Arg Ala Val

Glu Asp Gly Ile Asn Tyr Ala Thr Gly Asn Leu Pro Gly Cys Ser Phe 35 40 45

Ser Ile Phe Leu Leu Ala Leu Leu Ser Cys Leu Thr Val Pro Thr Ser

Ala Val Asn Tyr Arg Asn Ala Ser Gly Ile Tyr His Ile Thr Asn Asp 65 70 75 80

Cys Pro Asn Ala Ser Ile Val Tyr Glu Thr Glu Asn His Ile Leu His 85 90 95

Leu Pro Gly Cys Val Pro Cys Val Arg Thr Gly Asn Gln Ser Arg Cys 100 105 110

Trp Val Ala Leu Thr Pro Thr Val Ala Ser Pro Tyr Ala Gly Ala Pro 115 120 125

Leu Glu Pro Leu Arg Arg His Val Asp Leu Met Val Gly Ala Ala Thr 130 135 140 Met Cys Ser Ala Leu Tyr Ile Gly Asp Leu Cys Gly Gly Leu Phe Leu 145 150 155 160

Val Gly Gln Met Phe Thr Phe Gln Pro Arg Arg His Trp Thr Thr Gln 165 170 175

Asp Cys Asn Cys Ser Ile Tyr Thr Gly His Ile Thr Gly His Arg Met 180 185 190

Ala

- (2) INFORMATION FOR SEQ ID NO: 182:
 - (i) SEQUENCE CHARACTERISTICS:
 - (A) LENGTH: 192 amino acids
 - (B) TYPE: amino acid
 - (D) TOPOLOGY: linear
 - (ii) MOLECULE TYPE: protein
- (xi) SEQUENCE DESCRIPTION: SEQ ID NO: 182:

Ala Cys Gly Phe Ala Asp Leu Met Gly Tyr Ile Pro Leu Val Gly Ala 1 5 10 15

Pro Val Gly Gly Val Ala Arg Ala Leu Ala His Gly Val Arg Ala Val 20 25 30

Glu Asp Gly Ile Asn Tyr Ala Thr Gly Asn Leu Pro Gly Cys Ser Phe 35 40 45

Ser Ile Ser Phe Trp His Phe Ser Arg Ala * Leu Ser Arg Pro Arg 50 55 60

Leu Ser Thr Thr Gly Met Ser Arg Ala Ser Thr Thr Ser Pro Met Ile 65 70 75 80

Ala Arg Ile Pro Ala * Cys Met Lys Pro Ile Thr Thr Ser Cys Thr 85 90 95

Tyr Gln Gly Ala Tyr Pro Ala $\,\,^\star$ Gly Pro Gly Thr Phe Arg Ala Ala 100 $\,\,^\circ$ 105 110

Gly Tyr Leu * His Leu Leu Trp Leu Leu Pro Thr Ser Gly Leu Arg

Leu Arg Arg Tyr Gly Gly Met Trp Ile * Trp Trp Val Gln Pro Pro 130 135 140

Phe Ala Leu Pro Ser Thr Ser Glu Thr Ser Val Glu Val Ser Ser *
145 150 155 160

Trp Asp Arg Cys Ser Pro Ser Ser Arg Ala Ala Thr Gly Pro Leu Arg 165 170 175

Thr Ala Thr Ala Pro Phe Thr Ser Ala Thr Ser Gln Ala Thr Glu Trp

WO 94/2	25601	L				•		2	35				PC1/I	EP94/0.	1323
			180					185				190			
(2)	INFO	ORMA!	rion	FOR	SEQ	ID I	NO: :	185:							
	(i)	(1	A) Li 3) T	engti Ype : I'rani	HARAG H: 5' nuc: DEDNI DGY:	79 ba Leic ESS:	ase p acid	pair:	s						
	(ii)	MOI	ECUI	LE T	YPE:	CDN	A								
(:	iii)	нуі	POTH	ETIC	AL: 1	10									
(:	iii)	AN:	ri-si	ense	: NO										
	(ix)	(2		AME/I	KEY: ION:		579								
	(ix)	(2		ME/I	CEY:			tide							
	(xi)	SEÇ	ONEN	CE DI	SCR	PTIC	ON: S	SEQ :	ID NO): 1	35:				
ACT thr															48
Pro '															96
GAG Glu															144
TCT :															192
GCC Ala :															240
TGC (288
CTT															336

Trp	Val	Ala 115	Leu	ser	Pro	Thr	Val 120	Ala	Ala	Pro	Tyr	11e 125	Gly	Ala	Pro	
						CAC His 135				Met					ACT Thr	432
						ATT Ile										480
						TTC Phe										528
						TAC Tyr										576
GCA Ala																579

- (2) INFORMATION FOR SEQ ID NO: 186:
 - (i) SEQUENCE CHARACTERISTICS:
 - (A) LENGTH: 193 amino acids
 - (B) TYPE: amino acid (D) TOPOLOGY: linear
 - (ii) MOLECULE TYPE: protein
 - (xi) SEQUENCE DESCRIPTION: SEQ ID NO: 186:

Thr Cys Gly Phe Ala Asp Leu Met Gly Tyr Ile Pro Leu Val Gly Ala

Pro Val Gly Gly Val Ala Arg Ala Leu Glu His Gly Val Arg Ala Val 20 25 30

Glu Asp Gly Ile Asn Tyr Ala Thr Gly Asn Leu Pro Gly Cys Ser Phe

Ser Ile Tyr Leu Leu Ala Leu Leu Ser Cys Leu Thr Val Pro Thr Ser 50 55 60

Ala Ile His Tyr Arg Asn Ala Ser Gly Val Tyr His Val Thr Asn Asp 65 70 75 80

Cys Pro Asn Ser Ser Ile Val Tyr Glu Ala Asp His His Ile Leu His 85 90 95

Leu Pro Gly Cys Leu Pro Cys Val Arg Val Gly Asn Gln Ser Arg Cys 100 -105 110

Trp Val Ala Leu Ser Pro Thr Val Ala Ala Pro Tyr Ile Gly Ala Pro 115 120 125

								-	3/								
Va	130	Ser	Phe	Arg	Arg	His 135	Val	qaA	Met	Met	Val 140	Gly	Ala	Ala	Thr		
Va:	l Cys	Ser	Ala	Leu	Tyr 150	Ile	Gly	Asp	Leu	Cys 155	Gly	Gly	Val	Phe	Leu 160	•	
٧a.	l Gly	Gln	Met	Phe 165	Ser	Phe	Arg	Pro	Arg 170	Arg	His	Trp	Thr	Thr 175	Gln		
Asj	Cys	Asn	Сув 180		Ile	Tyr	Ala	Gly 185	His	Ile	Thr	Gly	His 190	Gly	Met		
Ala	ì																
(2)	INF	ORMA'	TION	FOR	SEQ	ID I	10: :	187:									
	(1)	(2	QUEN	ENGT	i: 5	79 ba	ase j	pair	9								
			B) T														
		(1	D) TO	OPOL	GY:	line	ear										
	(ii)	MO	LECU	LE T	PE:	cDN	4										
	(iii)	HY	ротн	BTIC	AL: 1	40											
	(iii)	AN.	ri-si	ENSE	: NO												
	(ix)	(2	ATURI A) Ni B) Lo	AME/I			579										
	(ix)	()	ATURI A) Ni B) Lo	AME/I				tide									
	(xi)	SEC	QUENC	CE DI	SCRI	IPTIC	on: s	SEQ :	ED NO): 1 8	37:						
	TGC Cys																48
	GTG Val																96
	GAC Asp															1	44
	ATC Ile 50															1	92
GCC	GTC	AAC	TAT	CGC	AAT	GCC	TCG	GGC	ATC	TAT	CAC	ATC	ACC	TAA	GAC	2	40

Ala 65	Val	Asn	Tyr	Arg	Asn 70	Ala	Ser	Gly	Ile	Tyr 75	His	Ile	Thr	Asn	qaA 08	
	CCG Pro															288
	CCA Pro															336
	GTG Val															384
	GAA Glu 130															432
	TGC Cys															480
	GGT Gly															528
	TGC Cys															576
GCA Ala																579

- (2) INFORMATION FOR SEQ ID NO: 188:
 - (i) SEQUENCE CHARACTERISTICS:
 - (A) LENGTH: 193 amino acids
 - (B) TYPE: amino acid
 - (D) TOPOLOGY: linear
 - (ii) MOLECULE TYPE: protein
 - (xi) SEQUENCE DESCRIPTION: SEQ ID NO: 188:

Thr Cys Gly Phe Ala Asp Leu Met Gly Tyr Ile Pro Leu Val Gly Ala

Pro Val Gly Val Ala Arg Ala Leu Ala His Gly Val Arg Ala Val $20 \ 25 \ 30$

Glu Asp Gly Ile Asn Tyr Ala Thr-Gly Asn Leu Pro Gly Cys Ser Phe \$35\$ \$40\$ \$45\$

Ser Ile Phe Leu Leu Ala Leu Leu Ser Cys Leu Thr Val Pro Thr Ser 50 55 60

Ala Val Asn Tyr Arg Asn Ala Ser Gly Ile Tyr His Ile Thr Asn Asp 65 70 75 80

Cys Pro Asn Ser Ser Ile Val Tyr Glu Thr Glu His His Ile Leu His 85 90 95

Leu Pro Gly Cys Leu Pro Cys Val Arg Val Gly Asn Gln Ser Arg Cys 100 105 110

Trp Val Ala Leu Thr Pro Thr Val Ala Ala Pro Tyr Ile Gly Ala Pro 115 120 125

Leu Glu Ser Leu Arg Ser His Val Asp Leu Met Val Gly Ala Ala Thr 130 135 140

Ala Cys Ser Ala Leu Tyr Ile Gly Asp Leu Cys Gly Gly Val Phe Leu 145 150 155 160

Val Gly Gln Met Phe Ser Phe Gln Pro Arg Arg His Trp Thr Thr Gln 165 170 175

Asp Cys Asn Cys Ser Ile Tyr Ala Gly His Val Thr Gly His Arg Met 180 185 190

Ala

- (2) INFORMATION FOR SEQ ID NO: 189:
 - (i) SEQUENCE CHARACTERISTICS:
 - (A) LENGTH: 579 base pairs
 - (B) TYPE: nucleic acid
 - (C) STRANDEDNESS: single (D) TOPOLOGY: linear
 - (ii) MOLECULE TYPE: cDNA
 - (iii) HYPOTHETICAL: NO
 - (iii) ANTI-SENSE: NO

 - (ix) FEATURE: (A) NAME/KEY: CDS
 - (B) LOCATION: 1..579
 - (ix) FEATURE:
 - (A) NAME/KEY: mat_peptide
 - (B) LOCATION: 1..576
 - (xi) SEQUENCE DESCRIPTION: SEO ID NO: 189:

ACS TGC GGC TTC GCC GAC CTC ATG GGA TAC ATC CCG CTC GTG GGC GCC
Thr Cys Gly Phe Ala Asp Leu Met Gly Tyr Ile Pro Leu Val Gly Ala
1 5 10

(2) INFORMATION FOR SEQ ID NO: 190:

GCG

Ala

- (i) SEQUENCE CHARACTERISTICS:
 - (A) LENGTH: 193 amino acids
 - (B) TYPE: amino acid
 - (D) TOPOLOGY: linear
- (ii) MOLECULE TYPE: protein

579

(xi) SEQUENCE DESCRIPTION: SEQ ID NO: 190:

Thr Cys Gly Phe Ala Asp Leu Met Gly Tyr Ile Pro Leu Val Gly Ala 1 $$ 5 $$ 10 $$ 15

Pro Val Gly Val Ala Arg Ala Leu Ala His Gly Val Arg Ala Val 20 25 30

Glu Asp Gly Ile Asn Tyr Ala Thr Gly Asn Leu Pro Gly Cys Ser Phe $35 \hspace{1cm} 40 \hspace{1cm} 45$

Ser Ile Phe Leu Leu Ala Leu Leu Ser Cys Leu Thr Val Pro Ala Ser 50 60

Ala Glu His Tyr Arg Asn Ala Ser Gly Ile Tyr His Ile Thr Asn Asp 65 70 75 80

Cys Pro Asn Ser Ser Val Val Tyr Glu Thr Asp His His Ile Leu His 85 90 95

Leu Pro Gly Cys Val Pro Cys Val Arg Ala Gly Asn Val Ser Arg Cys 100 105 110

Trp Thr Pro Val Thr Pro Thr Val Ala Ala Val Ser Met Asp Ala Pro 115 120 125

Leu Glu Ser Phe Arg Arg His Val Asp Leu Met Val Gly Ala Ala Thr 130 140

Val Cys Ser Val Leu Tyr Val Gly Asp Leu Cys Gly Gly Ala Phe Leu 145 \$150\$

Val Gly Gln Met Phe Thr Phe Gln Pro Arg Arg His Trp Thr Thr Gln 165 170 170

Asp Cys Asn Cys Ser Ile Tyr Thr Gly His Ile Thr Gly His Arg Met
180 185 190

- (2) INFORMATION FOR SEQ ID NO: 191:
 - (i) SEQUENCE CHARACTERISTICS:
 - (A) LENGTH: 289 base pairs
 - (B) TYPE: nucleic acid
 - (C) STRANDEDNESS: single
 - (D) TOPOLOGY: linear
 - (ii) MOLECULE TYPE: cDNA
 - (iii) HYPOTHETICAL: NO
 - (iii) ANTI-SENSE: NO
 - (ix) FEATURE:
 - (A) NAME/KEY: CDS

96

144

240

(B) LOCATION: 1..289

(ix)	FEATURE:

- (A) NAME/KEY: mat_peptide
 - (B) LOCATION: 1..286

(xi) SEQUENCE DESCRIPTION: SEQ ID NO: 191:

ATG AGC ACG AAT CCT AAA CCT CAA AGA AAA ACC AAA CGT AAC ACC AAC Met Ser Thr Asn Pro Lys Pro Gln Arg Lys Thr Lys Arg Asn Thr Asn

CGC CGC CCC ATG GAC GTT AAG TTC CCG GGC GGT GGC CAG ATC GTT GGT Arg Arg Pro Met Asp Val Lys Phe Pro Gly Gly Gly Gly Ile Val Gly

GGA GTT TAC TTG TTG CCG CGC AGG GGC CCC AGG TTG GGT GTG CGC GCG Gly Val Tyr Leu Leu Pro Arg Arg Gly Pro Arg Leu Gly Val Arg Ala

ACT AGG AAG ACT TCG GAG CGG TCG CAA CCT CGT GGG AGA CGT CAG CCT 192 Thr Arg Lys Thr Ser Glu Arg Ser Gln Pro Arg Gly Arg Arg Gln Pro 50 60

ATC CCC AAG GCA CGT CGA TCT GAG GGA AGG TCC TGG GCT CAG CCC GGG Ile Pro Lys Ala Arg Arg Ser Glu Gly Arg Ser Trp Ala Gln Pro Gly 65 70 80

TAC CCA TGG CCT CTT TAC GGT AAT GAG GGT TGT GGG TGG GCA GGA TGG G
TYr Pro Trp Pro Leu Tyr Gly Asn Glu Gly Cys Gly Trp Ala Gly Trp
85
90
95

(2) INFORMATION FOR SEO ID NO: 192:

- (i) SEQUENCE CHARACTERISTICS:
 - (A) LENGTH: 96 amino acids (B) TYPE: amino acid
 - (D) TOPOLOGY: linear
- (ii) MOLECULE TYPE: protein
- (xi) SEQUENCE DESCRIPTION: SEQ ID NO: 192:

Met Ser Thr Asn Pro Lys Pro Gln Arg Lys Thr Lys Arg Asn Thr Asn

Arg Arg Pro Met Asp Val Lys Phe Pro Gly Gly Gly Gln Ile Val Gly

Gly Val Tyr Leu Leu Pro Arg Arg Gly Pro Arg Leu Gly Val Arg Ala 35 40 45

Thr Arg Lys Thr Ser Glu Arg Ser Gln Pro Arg Gly Arg Arg Gln Pro

Ile Pro Lys Ala Arg Arg Ser Glu Gly Arg Ser Trp Ala Gln Pro Gly

65 70 75 80

Tyr Pro Trp Pro Leu Tyr Gly Asn Glu Gly Cys Gly Trp Ala Gly Trp 85 90 95

(2) INFORMATION FOR SEQ ID NO: 193:

(i) SEQUENCE CHARACTERISTICS:

- (A) LENGTH: 498 base pairs
- (B) TYPE: nucleic acid
- (C) STRANDEDNESS: single
 (D) TOPOLOGY: linear
- (ii) MOLECULE TYPE: cDNA
- (iii) HYPOTHETICAL: NO
- (iii) ANTI-SENSE: NO
- (ix) FEATURE:
 - (A) NAME/KEY: CDS (B) LOCATION: 1..498
- (ix) FEATURE:
 - (A) NAME/KEY: mat_peptide
 - (B) LOCATION: 1..495

(xi) SEQUENCE DESCRIPTION: SEQ ID NO: 193:

ATG	AGC	ACG	TAA	CCT	AAA	CCT	CAA	AGA	AAA	ACC	AAA	CGT	AAC	ACC	AAC	4.8	í
Met	Ser	Thr	Asn	Pro	Lys	Pro	Gln	Arg	Lys	Thr	Lys	Arg	Asn	Thr	Asn		
1				5					10					15			
CGC	CGC	CCT	ATG	GAC	GTA	AAG	TTC	CCG	GGC	GGT	GGA	CAG	ATC	GTT	GGC	96	í
Arg	Arg	Pro	Met	Asp	Val	Lys	Phe	Pro	Gly	Gly	Gly	Gln	Ile	Val	Gly		

GGA GTT TAC TTG TTG CCG CGC AGG GGC CCC CGG TTG GGT GTG CGC GCG GLY Val Tyr Leu Leu Pro Ard Ard Gly Pro Ard Leu Gly Val Ard Ala

35 40 45

ACT CGG AAG ACT TCG GAG CGG TCG CAA CCT CGT GGC AGG CGT CAA CCT 192

Thr Arg Lys Thr Ser Glu Arg Ser Gln Pro Arg Gly Arg Arg Gln Pro
50 60

ATC CCC AAG GCG CGC CGG TCC GAG GGC AGG TCC TGG GCG CAA GCC GGG 240

Ile Pro Lys Ala Arg Arg Ser Glu Gly Arg Ser Trp Ala Gln Ala Gly
65 70 78 80

TAC CCC TGG CCC CTC TAT GGC AAT GAG GGC TGT GGG TGG GCA GGG TGG

TYP Pro Trp Pro Leu Tyr Gly Asn Glu Gly Cys Gly Trp Ala Gly Trp

85
90
95

336

CTC CTG TCT CCT CGC GGC TCT CGG CCA TCT TGG GGC CCA AAT GAT CCC

Leu	Leu	Ser	Pro 100	Arg	Gly	Ser	Arg	Pro 105	Ser	Trp	Gly	Pro	Asn 110	Asp	Pro			
	CGG Arg															٠	384	
	TTC Phe 130																432	
	GGC Gly																480	
	ATT Ile																498	

- (2) INFORMATION FOR SEQ ID NO: 194:
 - (i) SEQUENCE CHARACTERISTICS:
 - (A) LENGTH: 166 amino acids
 - (B) TYPE: amino acid
 - (D) TOPOLOGY: linear
 - (ii) MOLECULE TYPE: protein
 - (xi) SEQUENCE DESCRIPTION: SEQ ID NO: 194:

Met Ser Thr Asn Pro Lys Pro Gln Arg Lys Thr Lys Arg Asn Thr Asn

1 5 10 . 15

Arg Arg Pro Met Asp Val Lys Phe Pro Gly Gly Gly Gln Ile Val Gly 20 25 30

Gly Val Tyr Leu Leu Pro Arg Arg Gly Pro Arg Leu Gly Val Arg Ala

Thr Arg Lys Thr Ser Glu Arg Ser Gln Pro Arg Gly Arg Arg Gln Pro

Ile Pro Lys Ala Arg Arg Ser Glu Gly Arg Ser Trp Ala Gln Ala Gly 65 70 75 80

Tyr Pro Trp Pro Leu Tyr Gly Asn Glu Gly Cys Gly Trp Ala Gly Trp 85 90 95

Leu Leu Ser Pro Arg Gly Ser Arg Pro Ser Trp Gly Pro Asn Asp Pro 100 105 110

Arg Arg Arg Ser Arg Asn Leu Gly Lys Val Ile Asp Thr Leu Thr Cys

Gly Phe Ala Asp Leu Met Gly Tyr Ile Pro Leu Val Gly Ala Pro Val 130 135 140

Gly Gly Val	Ala A	Arg Ala	Leu	Ala	His	Gly	Val	Arg	Ala	Val	Glu	Asp
145		150					155					160

Gly Ile Asn Tyr Arg Gln 165

(2) INFORMATION FOR SEQ ID NO: 195:

(i) SEQUENCE CHARACTERISTICS:

- (A) LENGTH: 579 base pairs
- (B) TYPE: nucleic acid
- (C) STRANDEDNESS: single
- (D) TOPOLOGY: linear
- (ii) MOLECULE TYPE: cDNA
- (iii) HYPOTHETICAL: NO
- (iii) ANTI-SENSE: NO

(ix) FEATURE:

(A) NAME/KEY: CDS (B) LOCATION: 1..579

(ix) FEATURE:

- (A) NAME/KEY: mat_peptide
- (B) LOCATION: 1..576

(xi) SEQUENCE DESCRIPTION: SEQ ID NO: 195:

	TGC Cvs															48
1	-2-	2		5	•			•	10					15	•	
	GTT															96
Pro	Val	Gly		Val	Ala	Arg	Ala		Ala	His	Gly	Val		Val	Leu	
			20					25					30			
GAG	GAC	GGG	GTG	AAT	TAT	GCA	ACA	GGG	AAT	CTG	CCT	GGT	TGC	TCT	TTC	144

Glu Asp Gly Val Asn Tyr Ala Thr Gly Asn Leu Pro Gly Cys Ser Phe 35 40 45

TCT ATC TTC ATT CTT GCA CTT CTC TCG TGC CTC ACT GTC CCG GCC TCT

Ser Ile Phe Ile Leu Ala Leu Leu Ser Cys Leu Thr Val Pro Ala Ser

50

55

60

GCA GTT CCC TAC CGA AAT GCC TCT GGG ATC TAT CAT GTC ACC AAT GAT
Ala Val Pro Tyr Arg Asn Ala Ser Gly Ile Tyr His Val Thr Asn Asp

TGC CCA AAC TCT TCC ATA GTC TAT GAG GCA GAT GAT CTG ATC CTA CAC
Cys Pro Asn Ser Ser Ile Val Tyr Glu Ala Asp Asp Leu Ile Leu His
85 90 95

GCA CCT GGC TGC GTG CCT TGT GTC AGG AAA GAT AAT GTG AGT AGG TGC

Ala	Pro	Gly	Cys 100	Val	Pro	Cys	Val	Arg 105	Lys	Asp	Asn	Val	Ser 110	Arg	Cys	
			ATT Ile													384
			CTT Leu													432
			GCG Ala													480
			ATG Met													528
			TGT Cys 180													576
GCA Ala																579
(0)																

- (2) INFORMATION FOR SEQ ID NO: 196:
 - (i) SEQUENCE CHARACTERISTICS:
 - (A) LENGTH: 193 amino acids
 - (B) TYPE: amino acid (D) TOPOLOGY: linear
 - (ii) MOLECULE TYPE: protein
 - (xi) SEQUENCE DESCRIPTION: SEQ ID NO: 196:

Thr Cys Gly Phe Ala Asp Leu Val Gly Tyr Ile Pro Leu Val Gly Gly
1 5 10 15

Pro Val Gly Gly Val Ala Arg Ala Leu Ala His Gly Val Arg Val Leu 20 25 30

Glu Asp Gly Val Asn Tyr Ala Thr Gly Asn Leu Pro Gly Cys Ser Phe

Ser Ile Phe Ile Leu Ala Leu Leu Ser Cys Leu Thr Val Pro Ala Ser 50 60

Ala Val Pro Tyr Arg Asn Ala Ser Gly Ile Tyr His Val Thr Asn Asp 65 70 75 80

Cys Pro Asn Ser Ser Ile Val Tyr Glu Ala Asp Asp Leu Ile Leu His 85 90 95

Ala Pro Gly Cys Val Pro Cys Val Arg Lys Asp Asn Val Ser Arg Cys
100 105 110

Trp Val Gln Ile Thr Pro Thr Leu Ser Ala Pro Ser Phe Gly Ala Val 115 120 125								
Thr Ala Pro Leu Arg Arg Ala Val Asp Tyr Leu Val Gly Gly Ala Ala 130 $$130$$								
Leu Cys Ser Ala Leu Tyr Val Gly Asp Ala Cys Gly Ala Leu Phe Leu 145 150 155 160								
Val Gly Gln Met Phe Thr Tyr Arg Pro Arg Gln His Ala Thr Val Gln 165 170 175								
Asp Cys Asn Cys Ser Ile Tyr Ser Gly His Val Thr Gly His Gln Met 180 185								
Ala								
A								
(2) INFORMATION FOR SEQ ID NO: 197:								
(i) SEQUENCE CHARACTERISTICS: (A) LENGTH: 579 base pairs (B) TYPE: nucleic acid (C) STRANDEDNESS: single (D) TOPOLOGY: linear								
(ii) MOLECULE TYPE: cDNA								
(iii) HYPOTHETICAL: NO								
(iii) ANTI-SENSE: NO								
(ix) FEATURE: (A) NAME/KEY: CDS								
(B) LOCATION: 1579								
Wal management								
(ix) FEATURE: (A) NAME/KEY: mat_peptide								
(B) LOCATION: 1576								
(xi) SEQUENCE DESCRIPTION: SEQ ID NO: 197:								
ACT TGC GGC TTT GCC GAC CTC ATG GGA TAC ATC CCG CTC GTA GGC GCC	48							
Thr Cys Gly Phe Ala Asp Leu Met Gly Tyr Ile Pro Leu Val Gly Ala								
1 5 10 15								
1 5 10 15 CCC GTG GGT GGC GTC GCC AGA GCC CTG GAA CAT GGT GTT AGG GCT GTG	96							
1 5 10 15	96							
1 5 10 15 CCC GTG GGT GGC GTC GCC AGA GCC CTG GAA CAT GGT GTT AGG GCT GTG Pro Val Gly Gly Val Ala Arg Ala Leu Glu His Gly Val Arg Ala Val 20 25 30	96 144							
1 5 10 15 CCC GTG GGT GGC GTC GCC AGA GCC CTG GAA CAT GGT GTT AGG GCT GTG Pro Val Gly Gly Val Ala Arg Ala Leu Glu His Gly Val Arg Ala Val 20 25 30								

Ser	Ile 50	Tyr	Leu	Leu	Ala	Leu 55	Leu	Ser	Cys	Leu	Thr 60	Val	Pro	Thr	ser	
	ATC															240
Ala	Ile	His	Tyr	Arg	Asn	Ala	Ser	Gly	Val	Tyr	His	Val	Thr	Asn	Asp	
65					70					75					80	
TGC	CCG	AAC	TCG	AGC	ATA.	GTG	TAC	GAG	GCC	GAC	CAC	CAC	ATC	CTA	CAC	288
Cys	Pro	Asn	Ser	Ser	Ile	Val	Tyr	Glu	Ala	Asp	His	His	Ile	Leu	His	
				85					90					95		
CTT	CCA	GGG	TGC	TTA	CCC	TGT	GTG	AGG	GTT	GGG	AAT	CAG	TCA	CGT	TGT	336
Leu	Pro	Gly	Сув	Leu	Pro	Cys	Val	Arg	Val	Gly	Asn	Gln	Ser	Arg	Cys	
			100					105					110			
	GTG															384
Trp	Val		Leu	Ser	Pro	Thr		Ala	Ala	Pro	Tyr		Gly	Ala	Pro	
		115					120					125				
	GAA															432
Val	Glu	Ser	Phe	Arg	Arg		Val	Asp	Met	Met		Gly	Ala	Ala	Thr	
	130					135					140					
	TGC															480
	Cys	Ser	Ala	Leu		Ile	Gly	Asp	Leu		Gly	Gly	Val	Phe		
145					150					155					160	
	GGT															528
Val	Gly	Gln	Met		Ser	Phe	Arg	Pro		Arg	His	Trp	Thr		Gln	
				165					170					175		
	TGC															576
Asp	Cys	Asn		Ser	Ile	Tyr	Ala		His	Ile	Thr	Gly		Gly	Met	
			180					185					190			
GCA																579
Ala																

- (2) INFORMATION FOR SEQ ID NO: 198:
 - (i) SEQUENCE CHARACTERISTICS:(A) LENGTH: 193 amino acids
 - (B) TYPE: amino acid
 - (D) TOPOLOGY: linear
 - (ii) MOLECULE TYPE: protein
 - (xi) SEQUENCE DESCRIPTION: SEQ ID NO: 198:

Thr Cys Gly Phe Ala Asp Leu Met Gly Tyr Ile Pro Leu Val Gly Ala $1 \hspace{1cm} 5 \hspace{1cm} 10 \hspace{1cm} 15$

Pro Val Gly Gly Val Ala Arg Ala Leu Glu His Gly Val Arg Ala Val

Glu Asp Gly Ile Asn Tyr Ala Thr Gly Asn Leu Pro Gly Cys Ser Phe

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45

35 40

Ser Ile Tyr Leu Leu Ala Leu Leu Ser Cys Leu Thr Val Pro Thr Ser 50 55 60

Ala Ile His Tyr Arg Asn Ala Ser Gly Val Tyr His Val Thr Asn Asp 65 70 75 80

Cys Pro Asn Ser Ser Ile Val Tyr Glu Ala Asp His His Ile Leu His 85 90 95

Leu Pro Gly Cys Leu Pro Cys Val Arg Val Gly Asn Gln Ser Arg Cys
100 105 110

Trp Val Ala Leu Ser Pro Thr Val Ala Ala Pro Tyr Ile Gly Ala Pro 115 120 125

Val Glu Ser Phe Arg Arg His Val Asp Met Met Val Gly Ala Ala Thr 130 135 140

Val Cys Ser Ala Leu Tyr Ile Gly Asp Leu Cys Gly Gly Val Phe Leu 145 · 150 155 160

Val Gly Gln Met Phe Ser Phe Arg Pro Arg Arg His Trp Thr Thr Gln 165 170 175

Asp Cys Asn Cys Ser Ile Tyr Ala Gly His Ile Thr Gly His Gly Met 180 $$185\ \ \, 190\ \ \,$

- (2) INFORMATION FOR SEQ ID NO: 199:
 - (i) SEQUENCE CHARACTERISTICS:
 - (A) LENGTH: 1470 base pairs
 - (B) TYPE: nucleic acid (C) STRANDEDNESS: single
 - (D) TOPOLOGY: linear
 - (ii) MOLECULE TYPE: cDNA
 - (iii) HYPOTHETICAL: NO
 - (iii) ANTI-SENSE: NO
 - (ix) FEATURE:
 - (A) NAME/KEY: CDS
 - (B) LOCATION: 2..1470
 - (ix) FEATURE:
 - (A) NAME/KEY: mat_peptide
 - (B) LOCATION: 2..1467
 - (xi) SEQUENCE DESCRIPTION: SEQ ID NO: 199:

WO 94/25601	250	PCT/EP94/0132	13
A TCA CCA CCG GAG CTT Ser Pro Pro Glu Leu	CTA TCA CAT ACT CCA CTT Leu Ser His Thr Pro Leu 10		46
TTG CTG ATG GAG GGT GT Leu Leu Met Glu Gly Va 20			94
ACG AGT GCC ATT CCC AG Thr Ser Ala Ile Pro Ar 35			142
TCC TTG ACC AGG CAG AGG Ser Leu Thr Arg Gln Arg 50			190
CGG CCA CCC CTC CCG GC Arg Pro Pro Leu Pro Ala 65	Val * Gln Arg Pro T		238
AAG TGG CCC TGC CTC AGG Lys Trp Pro Cys Leu Arg 80 8	Arg Gly Arg Phe Pro S		286
TTC CCC TTG CTT TTA TA Phe Pro Leu Leu * 100			334
CCA AGA AAA AAT GTG ATC Pro Arg Lys Asn Val Met 115			82
TGA ACG CCG TGG CAT AT * Thr Pro Trp His IIc	T ATA GAG GTC TAG ACG T Le Ile Glu Val * Thr S 135		.30
CAA CAG GAG ACG TGG TCG Gln Gln Glu Thr Trp Set 145	Cys Ala Ala Pro Thr A		178
TCA CCG GCG ACT TTG AT: Ser Pro Ala Thr Leu Ile 160 169	Leu Ser * Thr Ala T		26
AGA CGG TGG ACT TCA GTG Arg Arg Trp Thr Ser Va 180			74
CAG TGC CCC AGG ACG CAG Gln Cys Pro Arg Thr Gli 195			22
GGA GAG GTA GGC ACG GC Gly Glu Val Gly Thr Ala 210			70
CGT CTG GCA TGT TCG ACT			18

					,				
225			230			235			
Val		ATC Ile 245						TGC Cys 255	766
		CCC Pro							814
		GTT Val							862
		ACA Thr							910
		CTG Leu						CTG Leu	958
		ATG Met 325							1006
		TAC Tyr							1054
		ACC Thr							1102
		AGC Ser							1150
		TGC Cys							1198
		GGG Gly 405							1246
		GAT Asp							1294
		CGT Arg							1342
		ACG Thr							1390

		ACG														1438
Ala	Ala 465	Thr	Ser	Val	Trp	Asn 470	Lys	Ala	Glu	Gin	Phe 475	Trp	Pro	His	Thr	
TGT	GGA	ACT	TCA	TCA	GTG	GGA	TAC	AAT	AAT	AG						1470
Cys	Gly	Thr	Ser	Ser	Val	Gly	Tyr	Asn	Asn							

(2) INFORMATION FOR SEQ ID NO: 197:

(i) SEQUENCE CHARACTERISTICS:

- (A) LENGTH: 1485 base pairs
 - (B) TYPE: nucleic acid
- (C) STRANDEDNESS: single
- (D) TOPOLOGY: linear
- (ii) MOLECULE TYPE: cDNA

(ix) FEATURE:

- (A) NAME/KEY: CDS
- (B) LOCATION: 1..1485
- (xi) SEQUENCE DESCRIPTION: SEQ ID NO: 197:

TGTGCCAGGA	CCATCACCAC	CGGAGCTTCT	ATCACATACT	CCACTTACGG	CAAGTTCCTT	60	
GCTGATGGAG	GGTGTTCAGG	CGGCGCGCAT	GACGTGATCA	TATGCGACGA	GTGCCATTCC	120	
CAGGACGCCA	CCACCATTCT	TGGGATAGGC	ACTGTCCTTG	ACCAGGCAGA	GACGGCTGGA	180	
GCTAGGCTCG	TCGTCTTGGC	CACGGCCACC	CCTCCCGGCA	GTGTGACAAC	GCCCCACCCC	240	
AACATCGAGG	AAGTGGCCCT	GCCTCAGGAG	GGGGAGGTTC	CCTTCTACGG	CAGAGCCATT	300	
CCCCTTGCTT	TTATAAAGGG	TGGTAGGCAT	CTCATCTTCT	GCCATTCCAA	gaaaaaatgt	360	
GATGAACTCG	CCAAGCAACT	GACCAGCCTG	GGCGTGAACG	CCGTGGCATA	TTATAGAGGT	420	
CTAGACGTCG	CCGTCATACC	CACAACAGGA	GACGTGGTCG	TGTGCAGCAC	CGACGCGCTC	480	
ATGACGGGAT	TCACCGGCGA	CTTTGATTCT	GTCATAGACT	GCAACTCCGC	CGTCACTCAG	540	
ACGGTGGACT	TCAGTCTGGA	TCCCACTTTT	ACCATTGAGA	CTACCACAGT	GCCCCAGGAC	600	
GCAGTGTCCA	GAAGCCAGCG	TTGGGGCCGC	ACGGGGAGAG	GTAGGCACGG	CATATACCGG	660	
TATGTCTCGG	CTGGAGAGAG	ACCGTCTGGC	ATGTTCGACT	CCGTGGTGCT	CTGTGAGTGC	720	
TACGATGCCG	GATGTGCATG	GTACGATCTG	ACTCCTGCCG	AGACTACCGT	GAGGTTGCGC	780	
GCTTACNTAA	ACACCCCCGG	GCTCCCTGTC	TGTCAGGACC	ATTTGGAATT	CTGGGAGGG	840	
GTGTTCACGG	GGCTCACTAA	CATCGACGCT	CACATGCTGT	CACAGACCAA	ACAGGGTGGG	900	
GAGAATTTCC	CATACCTTGT	AGCGTACCAA	GCAACAGTCT	GTGTTCGCGC	GAAAGCGCCC	960 '	

CCCCCAGCT	GGGACACAAT	GTGGAAATGC	ATGCTCCGTC	TCAAACCGAC	NTTAACTGGC	1020
CCTACTCCCC	TCTTGTACAG	GCTGGGGCCC	GTCCAGAATG	AGATCACACT	GACGCACCCC ·	1080
ATCACCAAGT	ACATTATGGC	TTGCATGTCT	GCGGACTTGG	AGGTCATTAC	CAGCACTTGG	1140
GTTCTGGTGG	GGGGCGTTGT	GGCGGCCCTG	GCGGCCTACT	GCTTGACGGT	GGGTTCGGTA	1200
GCCATAGTCG	GTAGGATCAT	CCTCTCTGGG	AAACCTGCCA	TCATTCCCGA	TAGGGAGGTA	1260
TTATACCAGC	aatttgatga	GATGGAGGAG	TGCTCGGCCT	CGTTGCCCTA	TATGGACGAA	1320
ACACGTGCCA	TTGCCGGACA	ATTCAAAGAG	AAAGTGCTCG	GCTTCATCAG	CACGACCGGC	1380
CAGAAGGCTG	AAACTCTGAA	GCCGGCAGCC	ACGTCTGTGT	GGAACAAGGC	TGAGCAGTTC	1440
TGGNCCACAT	ACATGTGGAA	CTTCATCAGT	GGGATACAAT	AATAG		1485
(0)						

- (2) INFORMATION FOR SEQ ID NO: 198:
 - (i) SEQUENCE CHARACTERISTICS:
 - (A) LENGTH: 484 amino acids
 - (B) TYPE: amino acid
 - (C) STRANDEDNESS: single
 - (D) TOPOLOGY: linear
 - (ii) MOLECULE TYPE: protein
 - (xi) SEQUENCE DESCRIPTION: SEQ ID NO: 198:
 - Cys Ala Arg Thr Ile Thr Thr Gly Ala Ser Ile Thr Tyr Ser Thr Tyr 1 5 10 15
 - Gly Lys Phe Leu Ala Asp Gly Gly Cys Ser Gly Gly Ala His Asp Val $20 \\ 25 \\ 30$
 - Ile Ile Cys Asp Glu Cys His Ser Gln Asp Ala Thr Thr Ile Leu Gly $35 \hspace{1cm} 40 \hspace{1cm} 45$
 - Ile Gly Thr Val Leu Asp Gln Ala Glu Thr Ala Gly Ala Arg Leu Val 50 60
 - Val Leu Ala Thr Ala Thr Pro Pro Gly Ser Val Thr Thr Pro His Pro 65 70 70 80 80
 - Asn Ile Glu Glu Val Ala Leu Pro Gln Glu Glu Glu Val Pro Phe Tyr 85 90 95
 - Gly Arg Ala Ile Pro Leu Ala Phe Ile Lys Gly Gly Arg His Leu Ile 100 105 110
 - Phe Cys His Ser Lys Lys Lys Cys Asp Glu Leu Ala Lys Gln Leu Thr 115 120 125
 - Ser Leu Gly Val Asn Ala Val Ala Tyr Tyr Arg Gly Leu Asp Val Ala 130 135 140

Val 145	Ile	Pro	Thr	Thr	Gly 150	Asp	Val	Va1	Val	Сув 155	ser	Thr	Asp	Ala	Leu 160
Met	Thr	Gly	Phe	Thr 165	Gly	Asp	Phe	Авр	Ser 170	Val	Ile	Asp	Cys	Asn 175	Ser
Ala	Val	Thr	Gln 180	Thr	Val	Asp	Phe	Ser 185	Leu	Asp	Pro	Thr	Phe 190	Thr	Ile
Glu	Thr	Thr 195	Thr	Val	Pro	Gln	Asp 200	Ala	Val	Ser	Arg	Ser 205	Gln	Arg	Trp
Gly	Arg 210	Thr	Gly	Arg	Gly	Arg 215	His	Gly	Ile	Tyr	Arg 220	Tyr	Val	Ser	Ala
Gly 225	Glu	Arg	Pro	Ser	Gly 230	Met	Phe	Asp	Ser	Val 235	Val	Leu	Cys	Glu	Cys 240
Tyr	Asp	Ala	Gly	Cys 245	Ala	Trp	Tyr	Asp	Leu 250	Thr	Pro	Ala	Glu	Thr 255	Thr .
Val	Arg	Leu	Arg 260	Ala	Tyr	Xaa	Asn	Thr 265	Pro	Gly	Leu	Pro	Val 270	Cys	Gln
Asp	His	Leu 275	Glu	Phe	Trp	Glu	Gly 280	Val	Phe	Thr	Gly	Leu 285	Thr	Asn	Ile
Asp	Ala 290	His	Met	Leu	Ser	Gln 295	Thr	Lys	Gln	Gly	Gly 300	Ġlu	Asn	Phe	Pro
Tyr 305	Leu	Val	Ala	Tyr	Gln 310	Ala	Thr	Val	Cys	Val 315	Arg	Ala	Lys	Ala	Pro 320
Pro	Pro	Ser	Trp	Asp 325	Thr	Met	Trp	Lys	Cys 330	Met	Leu	Arg	Leu	Lys 335	Pro
Xaa	Leu	Thr	Gly 340	Pro	Thr	Pro	Leu	Leu 345	Tyr	Arg	Leu	Gly	Pro 350	Val	Gln
Asn	Glu	Ile 355	Thr	Leu	Thr	His	Pro 360	Ile	Thr	Lys	Tyr	Ile 365	Met	Ala	Cys
	370		·		Glu	375					380				•
385					Leu 390					395					400
			-	405	Ile				410	-				415	
Asp	Arg	Glu	Val 420	Leu	Tyr	Gln	Gln	Phe 425	Asp	Glu	Met	Glu	Glu 430	Сув	Ser
Ala	ser	Leu 435	Pro	Tyr	Met	Asp	Glu 440	Thr	Arg	Ala	Ile	Ala 445	Gly	Gln	Phe

Lys Glu Lys Val Leu Gly Phe 11e Ser Thr Thr Gly Gln Lys Ala Glu 450 455 460

Thr Leu Lys Pro Ala Ala Thr Ser Val Trp Asn Lys Ala Glu Gln Phe 465 470 475 480

Trp Xaa Thr Tyr

(2) INFORMATION FOR SEQ ID NO: 199:

(i) SEQUENCE CHARACTERISTICS:

- (A) LENGTH: 1485 base pairs
 - (B) TYPE: nucleic acid
 - (C) STRANDEDNESS: single
 - (D) TOPOLOGY: linear

(ii) MOLECULE TYPE: cDNA

(ix) FEATURE:

- (A) NAME/KEY: CDS
 - (B) LOCATION: 1..1485

(xi) SEQUENCE DESCRIPTION: SEQ ID NO: 199:

TGTGCCAGGA CCATCACCAC CGGAGCTTCT ATCACATACT CCACTTACGG CAAGTTCCTT 60 GCTGATGGAG GGTGTTCAGG CGGCGCGTAT GACGTGATCA TATGCGACGA GTGCCATTCC CAGGACGCCA CCACCATTCT TGGGATAGGC ACTGTCCTTG ACCAGGCAGA GACGGCTGGA 180 GCTAGGCTCG TCGTCTTGGC CACGGCCACC CCTCCCGGCA GTGTGACAAC GCCCCACCCC 240 AACATCGAGG AAGTGGCCCT GCCTCAGGAG GGGGAGGTTC CCTTCTACGG CAGAGCCATT 300 CCCCTTGCTT TTATAAAGGG TGGTAGGCAT CTCATCTTCT GCCATTCCAA GAAAAAATGT GATGAACTCG CCAAGCAACT GACCAGCCTG GGCGTGAACG CCGTGGCATA TTATAGAGGT 420 CTAGACGTCG CCGTCATCCC CACAGCAGGA GACGTGGTCG TGTGCAGCAC CGACGCGCTC 480 ATGACGGGAT TCACCGGCGA CTTTGATTCT GTCATAGACT GCAACTCCGC CGTCACTCAG 540 ACGGTGGACT TCAGTCTGGA TCCCACTTTT ACCATTGAGA CTACCACAGT GCCCCAGGAC 600 GCAGTGTCCA GAAGCCAGCG TAGGGGCCGC ACGGGGAGAG GTAGGCACGG CATATACCGG 660 TATGTCTCGG CTGGAGAGAG ACCNTCTGAC ATGTTCGACT CCGTGGTGCT CTGTGAGTGC 720 TACGATGCCG GATGTGCGTG GTATGATCTG ACTCCTGCCG AGACTACCGT GAGGTTGCGC 780 GCTTACATAA ACACCCCGG GCTCCCTGTC TGTCAGGACC ATTTGGAATT CTGGGAGGG 840 GTGTTCACGG GGCTCACTAA CATCGACGCT CACATGCTGT CACAGACCAA ACAGGGTGGG 900 GAGAATTING CATACCTIGT AGCGTACCAA GCAACAGTCT GTGTTCGCGC GAAAGCGCCC 960

CCCCCCAGCT	GGGACACAAT	GTGGAAATGC	ATGCTCCGTC	TCAAACCGAC	TTTAACTGGC	1020
CCTACTCCCC	TCTTGTACAG	GCTGGGGCCC	GTCCAGANTG	AGATCACACT	GACGCACCCC	1080
ATCACCAAGT	ACATTATGGC	TTGCATGTCT	GCGGACTTGG	AGGTCATTAC	CANCACTTGG	1140
GTTCTGGTGG	GGGGCGTTGT	GGCGGCCCTG	GCGGCCTACT	GCTTGACGGT	GGGTTCGGTA	1200
GCCATAGTCG	GTAGGATCAT	CCTCTCTGGG	AAACCTGCCA	TCATTCCCGA	TAGGGAGGCA	1260
TTATACCAGC	aatttgatga	GATGGAGGAG	TGCTCGGCCT	CGTTGCCCTA	TATGGACGAG	1320
ACACGTGCCA	TTGCCGGACA	ATTCAAAGAG	AAAGTGCTCG	GCTTCATCAG	CACGACCGGC	1380
CAGAAGGCTG	AAACTCTGAA	GCCGGCAGCC	ACGTCTGTGT	GGAACAAGGC	TGAGCAGTTC	1440
TGGGCCACAT	ACATGTGGAA	CTTCATCAGC	GGGATACAAT	AATAG		1485

(2) INFORMATION FOR SEQ ID NO: 200:

- (i) SEQUENCE CHARACTERISTICS:
 - (A) LENGTH: 484 amino acids
 - (B) TYPE: amino acid
 - (C) STRANDEDNESS: single
 - (D) TOPOLOGY: linear
- (ii) MOLECULE TYPE: protein
- (xi) SECUENCE DESCRIPTION: SEO ID NO: 200:
- Cys Ala Arg Thr Ile Thr Thr Gly Ala Ser Ile Thr Tyr Ser Thr Tyr 15 -
- Gly Lys Phe Leu Ala Asp Gly Gly Cys Ser Gly Gly Ala Tyr Asp Val
- Ile Ile Cys Asp Glu Cys His Ser Gln Asp Ala Thr Thr Ile Leu Gly
- Ile Gly Thr Val Leu Asp Gln Ala Glu Thr Ala Gly Ala Arg Leu Val
- Val Leu Ala Thr Ala Thr Pro Pro Gly Ser Val Thr Thr Pro His Pro
- Asn Ile Glu Glu Val Ala Leu Pro Gln Glu Gly Glu Val Pro Phe Tyr 85 90
- Gly Arg Ala Ile Pro Leu Ala Phe Ile Lys Gly Gly Arg His Leu Ile 105
- Phe Cys His Ser Lys Lys Cys Asp Glu Leu Ala Lys Gln Leu Thr 115 120

 001							257						_		
Ser	Leu 130	Gly	Val	Asn	Ala	Val 135	Ala	Tyr	Tyr	Arg	Gly 140	Leu	Asp	Val	Ala
Val 145	Ile	Pro	Thr	Ala	Gly 150	Asp	Val	Val	Val	Cys 155	Ser	Thr	Asp	Ala	Leu 160
Met	Thr	Gly	Phe	Thr 165	Gly	Asp	Phe	Asp	Ser 170	Val	Ile	Asp	Cys	Asn 175	Ser
Ala	Val	Thr	Gln 180	Thr	Val	Asp	Phe	Ser 185	Leu	Asp	Pro	Thr	Phe 190	Thr	Ile
Glu	Thr	Thr 195	Thr	Val	Pro	Gln	Asp 200	Ala	Val	Ser	Arg	Ser 205	Gln	Arg	Arg
Gly	Arg 210	Thr	Gly	Arg	Gly	Arg 215	His	Gly	Ile	Tyr	Arg 220	Tyr	Val	Ser	Ala
31y 225	Glu	Arg	Xaa	Ser	Asp 230	Met	Phe	Asp	Ser	Val 235	Val	Leu	Сув	Glu	Cys 240
Fyr	Asp	Ala	Gly	Cys 245	Ala	Trp	Tyr	Asp	Leu 250	Thr	Pro	Ala	Glu	Thr 255	Thr
Val	Arg	Leu	Arg 260	Ala	Tyr	Ile	Asn	Thr 265	Pro	Gly	Leu	Pro	Val 270	Cys	Gln
Asp	His	Leu 275	Glu	Phe	Trp	Glu	Gly 280	Val	Phe	Thr	Gly	Leu 285	Thr	Asn	Ile
Asp	Ala 290	His	Met	Leu	Ser	Gln 295	Thr	Lys	Gln	Gly	Gly 300	Glu	Asn	Xaa	Pro
Tyr 305	Leu	Val	Ala	Tyr	Gln 310	Ala	Thr	Val	Cys	Val 315	Arg	Ala	Lys	Ala	Pro 320
Pro	Pro	ser	Trp	Asp 325	Thr	Met	Trp	Lys	Сув 330	Met	Leu	Arg	Leu	Lys 335	Pro
Fhr	Leu	Thr	Gly 340	Pro	Thr	Pro	Leu	Leu 345	Tyr	Arg	Leu	Gly	Pro 350	Val	Gln
Kaa	Glu	Ile 355	Thr	Leu	Thr	His	Pro 360	Ile	Thr	Lys	Tyr	Ile 365	Met	Ala	Cys
	370		Asp			375					380				
385			Ala		390					395					400
			Gly	405					410					415	
Asp	Arg	Glu	Ala 420	Leu	Tyr	Gln	Gln	Phe 425	Asp	Glu	Met	Glu	Glu 430	Cys	Ser

Ala Ser Leu Pro Tyr Met Asp Glu Thr Arg Ala Ile Ala Gly Gln Phe

			43	5				44	0				44	5			
	Ly	s Gl 45	u Ly 0	s Va	l Le	u Gl	y Ph 45		e Se	r Th	r Th	r G1 46		n Ly	rs Ala	Glu	
	Th 46	r Le 5	u Ly	s Pr	o Al	a Al 47		r Se	r Va	l Tr	p As 47		s Al	a G	u Gln	Phe 480	
(2)	Tr			r Ty FOR		ID:	NO:	201:									
	(i	(.	A) L B) T C) S	CE C ENGT: YPE: TRAN	H: 3 nuc DEDN	40 b leic ESS:	ase aci sin	pair d	s								
	(ii)	MO	LECU	LE T	YPE:	cDN	A.										
	(iii)	HY	POTH	ETIC	AL:	NO.											
	(iii)	AN	ri-s	ense	: NO												
	(ix)	()		E: AME/I OCAT:			340										
	(ix)	()		E: AME/I OCAT:				tide									
	(x1)	SE	QUEN	CE DI	BSCR:	PTIC	ON:	SEQ :	ID N	0: 2	01:						
	CC AC								rg V					al T			46
	TGT Cys														CTC Leu		94
	GAG Glu														GAC Asp		142
	TGC Cys														AGC Ser		190
	GGG Gly 65														AGG Arg		238
	GCG Ala														TTA Leu 95		286

GTC GTG ATC GCT GAA AGC GGT GGC GTC GAG GAG GAC AAG CGA GCC CTC Val Val Ite Ala Giu Ser Gly Gly Val Glu Glu Asp Lys Arg Ala Leu 100 105 105 110

334

GGA GCT Glv Ala 340

- (2) INFORMATION FOR SEO ID NO: 202:
 - (i) SEQUENCE CHARACTERISTICS:
 - (A) LENGTH: 113 amino acids
 - (B) TYPE: amino acid (D) TOPOLOGY: linear
 - (ii) MOLECULE TYPE: protein
 - (xi) SEQUENCE DESCRIPTION: SEQ ID NO: 202:

Ser Thr Val Thr Glu Arg Asp Ile Arg Val Glu Glu Val Tyr Gln

1 5 10 15 Cys Cys Asp Leu Glu Pro Glu Ala Arg Lys Val Ile Thr Ala Leu Thr

Glu Arg Leu Tyr Val Gly Gly Pro Met Tyr Asn Ser Lys Gly Asp Leu

Cys Gly Tyr Arg Arg Cys Arg Ala Ser Gly Val Tyr Thr Thr Ser Phe

Gly Asn Thr Leu Thr Cys Tyr Leu Lys Ala Ser Ala Ala Ile Arg Ala

Ala Gly Leu Lys Asp Cys Thr Met Leu Val Cys Gly Asp Asp Leu Val

Val Ile Ala Glu Ser Gly Gly Val Glu Glu Asp Lys Arg Ala Leu Gly
100 105 110

Ala

- (2) INFORMATION FOR SEQ ID NO: 203:
 - (i) SEQUENCE CHARACTERISTICS:
 - (A) LENGTH: 340 base pairs
 - (B) TYPE: nucleic acid
 - (C) STRANDEDNESS: single
 - (D) TOPOLOGY: linear
 - (ii) MOLECULE TYPE: cDNA
 - (iii) HYPOTHETICAL: NO
 - -
 - (iii) ANTI-SENSE: NO

	(ix)		() N2	AME/	KEY:		340									
	(ix)) N2	AME/	KEY: ION:			tide								
	(xi)	SEQ	UENC	E D	ESCR:	IPTI	ON:	SEQ :	ID N	0: 2	03:					
	TCC AC Ser Th								rg V					al T		46
	G TGT n Cys															94
	T GAA r Glu													GGA		142
	A TGC u Cys															190
	C GGG e Gly 65															238
Al	C GCT a Ala 0															286
GT	C GTT	ATC	GCC	GAA	AGC	GAT	GGT	GTC	GAA	GAG	GAC	CGC	CGA	GCC	CTC	334

(2) INFORMATION FOR SEQ ID NO: 204:

100

GGA GCT

Gly Ala

- (i) SEQUENCE CHARACTERISTICS:
 - (A) LENGTH: 113 amino acids
 - (B) TYPE: amino acid
 - (D) TOPOLOGY: linear
- (ii) MOLECULE TYPE: protein
- (xi) SEQUENCE DESCRIPTION: SEQ ID NO: 204:

Ser Thr Val Thr Glu Arg Asp Ile Arg Val Glu Glu Glu Val Tyr Gln

1 10 15

Val Val Ile Ala Glu Ser Asp Gly Val Glu Glu Asp Arg Arg Ala Leu

105

110

340

Cys Cys Asp Leu Glu Pro Glu Thr Arg Lys Val Ile Ser Ala Leu Thr 20 25 30

Glu Arg Leu Tyr Val Gly Gly Pro Met His Asn Ser Arg Gly Asp Leu 35 40 45

Cys Gly Tyr Arg Arg Cys Arg Ala Ser Gly Val Tyr Thr Thr Ser Phe 50 55 60

Gly Asn Thr Leu Thr Cys Phe Leu Lys Ala Thr Ala Ala Thr Lys Ala 65 70 75 80

Ala Gly Leu Lys Asp Cys Thr Met Leu Val Cys Gly Asp Asp Leu Val 85 90 95

Val Ile Ala Glu Ser Asp Gly Val Glu Glu Asp Arg Arg Ala Leu Gly 100 105 110

Ala

- (2) INFORMATION FOR SEO ID NO: 205:
 - (i) SEQUENCE CHARACTERISTICS:
 - (A) LENGTH: 340 base pairs
 - (B) TYPE: nucleic acid
 - (C) STRANDEDNESS: single
 - (D) TOPOLOGY: linear
 - (ii) MOLECULE TYPE: cDNA
 - (iii) HYPOTHETICAL: NO
 - (iii) ANTI-SENSE: NO
 - (ix) FEATURE:
 - (A) NAME/KEY: CDS
 - (B) LOCATION: 2..340
 - (ix) FEATURE:
 - (A) NAME/KEY: mat_peptide
 - (B) LOCATION: 2..337
 - (xi) SEQUENCE DESCRIPTION: SEQ ID NO: 205:

C TCC ACG GTG ACC GAA AGG GAT ATC AGG ACC GAG GAA GAG ATC TAC Ser Thr Val Thr Glu Arg Asp Ile Arg Thr Glu Glu Glu Ile Tyr 1 5 10 15

CAG TGC TGC GAC CTG GAG CCC GAA GCC CGC AAG GTG ATA TCC GCC CTA Gln Cys Cys Asp Leu Glu Pro Glu Ala Arg Lys Val Ile Ser Ala Leu 20 25 30

ACG GAA AGA CTC TAC GTG GGC GGT CCC ATG TAC AAC TCC AAG GGG GAC

Thr Glu Arg Leu Tyr Val Gly Gly Pro Met Tyr Aen Ser Lys Gly Asp

35

40

45

CTA	TGC	GGG	CAA	CGG	AGG	TGC	CGC	GCA	AGC	GGG	GTC	TAC	ACC	ACC	AGC	190
Leu	Cys	Gly	Gln	Arg	Arg	Cys	Arg	Ala	ser	Gly	val	Tyr	Thr	Thr	ser	
		50					55					60				
TTC	GGG	AAC	ACT	GTA	ACG	TGT	TAT	CTC	AAG	GCC	GTT	GCG	GCT	ACT	AGG	238
Phe	Gly	Asn	Thr	Val	Thr	Сув	Tyr	Leu	Lys	Ala	Val	Ala	Ala	Thr	Arg	
	65					70	-				75					
GCC	GCA	GGT	CTG	AAA	GGT	TGC	AGC	ATG	CTG	GTT	TGT	GGA	GAC	GAC	TTA	286
Ala	Ala	Gly	Leu	Lys	Gly	Cys	Ser	Met	Leu	Val	Cys	Gly	Asp	Asp	Leu	
80		•		•	85	-				90	-	_	_	-	95	
GTC	GTC	ATC	TGC	GAG	AGC	GGC	GGC	GTA	GAG	GAG	GAT	GCA	AGA	GCC	CTC	334
Val	Val	Ile	Cys	Glu	Ser	Gly	Gly	Val	Glu	Glu	Asp	Ala	Arg	Ala	Leu	
			-	100			-		105					110		
CGA	GCC															340
Arg	Ala															

(2) INFORMATION FOR SEQ ID NO: 206:

- (i) SEQUENCE CHARACTERISTICS:
 - (A) LENGTH: 113 amino acids
 - (B) TYPE: amino acid
 - (D) TOPOLOGY: linear
- (ii) MOLECULE TYPE: protein
- (xi) SEQUENCE DESCRIPTION: SEQ ID NO: 206:

Ser Thr Val Thr Glu Arg Asp Ile Arg Thr Glu Glu Glu Ile Tyr Gln 1 5 10 15

Cys Cys Asp Leu Glu Pro Glu Ala Arg Lys Val Ile Ser Ala Leu Thr 20 25 30

Glu Arg Leu Tyr Val Gly Gly Pro Met Tyr Asn Ser Lys Gly Asp Leu 35 40 45

Cys Gly Gln Arg Arg Cys Arg Ala Ser Gly Val Tyr Thr Thr Ser Phe 50 55 60

Gly Asn Thr Val Thr Cys Tyr Leu Lys Ala Val Ala Ala Thr Arg Ala 65 75 80

Ala Gly Leu Lys Gly Cys Ser Met Leu Val Cys Gly Asp Asp Leu Val 85 90 95

Val Ile Cys Glu Ser Gly Gly Val Glu Glu Asp Ala Arg Ala Leu Arg 100 105 110

Ala

(2) INFORMATION FOR SEQ ID NO: 207:

(i) SEQUENCE CHARACTERISTICS:

(A) LENGTH: 340 base pairs

(B) TYPE: nucleic acid

(C) STRANDEDNESS: single (D) TOPOLOGY: linear	•
(ii) MOLECULE TYPE: cDNA	
(iii) HYPOTHETICAL: NO	
(iii) ANTI-SENSE: NO	
(ix) FEATURE: (A) NAME/KEY: CDS (B) LOCATION: 2340	
<pre>(ix) FEATURE: (A) NAME/KEY: mat_peptide (B) LOCATION: 2337</pre>	
(xi) SEQUENCE DESCRIPTION: SEQ ID NO: 207:	
C TCC ACG GTG ACT GAA AGG GAC ATT AGG GTC GAG GAA GAG ATC TAG Ser Thr Val Thr Glu Arg Asp Ile Arg Val Glu Glu Glu Ile Tyr	2 46
1 5 10 15	
CAG TGC TGT GAC CTG GAG CCC GAG GCA CGC AAG GTG ATA TCC GCT CGC CGC Cys Asp Leu Glu Pro Glu Ala Arg Lys Val Ile Ser Ala I 20 25 30	CTC 94 Leu
ACA GAA AGA CTC TAC AAG GGC GGC CCC ATG TAT AAC AGC AAG GGG GG Thr Glu Arg Leu Tyr Lys Gly Gly Pro Met Tyr Asn Ser Lys Gly A 35 $40 \qquad \qquad 45$	BAC 142 Asp
CTA TGC GGG CTT CGG AGG TGC CGC GCA AGC GGG GTA TAC ACC ACA R Leu Cys Gly Leu Arg Arg Cys Arg Ala Ser Gly Val Tyr Thr Thr S 50 55 60	
TTC GGG AAC ACG GTG ACA TGC TAC CTT AAA GCC ACA GCA GCC ACC A Phe Gly Asn Thr Val Thr Cys Tyr Leu Lys Ala Thr Ala Ala Thr A 65 70 75	ugg 238 urg
GCT GCA GGG CTG AAA GAT TGC ACT ATG CTG GTA TGC GGT GAC GAC T Ala Ala Gly Leu Lys Asp Cys Thr Met Leu Val Cys Gly Asp Asp L 80 90	TA 286 eu 95
GTC GTT ATT GCC GAA AGC GGT GGC GTG GAG GAG GAC GCC CGA GCC C Val Val Ile Ala Glu Ser Gly Gly Val Glu Glu Asp Ala Arg Ala L 100 105 110	
CGA GCC Arg Ala	340

O 94/	25601							2	,	PCT/EP					
		() ()	SEQUI A) LI B) T D) T LECUI	ENGTI YPE: OPOLO	amii GY:	13 an no ao line	nino cid sar	acio							
	(~1)	000	OUEN	ים שי	ecp.	TOTT	ONT.	GEO .	n N)· 20	18+				
Ser 1			Thr									Glu	Ile	Tyr 15	Gln
Cys	Cys	Asp	Leu 20	Glu	Pro	Glu	Ala	Arg 25	Lys	Val	Ile	Ser	Ala 30	Leu	Thr
Glu	Arg	Leu 35	Tyr	Lys	Gly	Gly	Pro 40	Met	Tyr	Asn	Ser	Lys 45	Gly	Asp	Leu
Cys	Gly 50	Leu	Arg	Arg	Cys	Arg 55	Ala	Ser	Gly	Val	Tyr 60	Thr	Thr	Ser	Phe
Gly 65	Asn	Thr	Val	Thr	Cys 70	Tyr	Leu	Lys	Ala	Thr 75	Ala	Ala	Thr	Arg	Ala 80
Ala	Gly	Leu	Lys	Asp 85	Сув	Thr	Met	Leu	Val 90	Cys	Gly	Asp	Asp	Leu 95	Val
Val	Ile	Ala	Glu 100	Ser	Gly	Gly	Val	Glu 105	Glu	Asp	Ala	Arg	Ala 110	Leu	Arg
Ala															
(2)			rion		-										
	(i)		QUEN												

Ala

- (2) I

 - (B) TYPE: nucleic acid (C) STRANDEDNESS: single
 - (D) TOPOLOGY: linear
 - (ii) MOLECULE TYPE: cDNA
 - (iii) HYPOTHETICAL: NO
 - (iii) ANTI-SENSE: NO

 - (ix) FEATURE:
 - (A) NAME/KEY: CDS (B) LOCATION: 1..340
 - (xi) SEQUENCE DESCRIPTION: SEQ ID NO: 209:

CCCCACCGTG ACNGAGAGGG ACNTCAGGGT CGAGGAAGAG GTCTATCAGT GCTGTAATCT

GGAGNCCGAT GNCCGCAAGG TCATCAACGC CCTCACAGAG AGACTCTACG TGGGCGGCCC

TATGCACA	AC A	GCAA	ggga(g ac	CTGT	ЭTGG	CAT	CCGT	AGA '	TGCC	3CGC	ga g	CGGC	3TTT2	A	180
CACCACGA	GC T	TCGG	AAAC	A CG	CTGA	CTTG	CTA	CCTC	AAA	3CCA	CAGC	GG C	CACC	AGGG	2 -	240
CGCGGGCT	TG A	AGGA'	TTGC	A CC	ATGC	rggt	CTG	CGGN	JAC (GACC'	rggt	rg T	CATT	3CTG2	A	300
GAGCATTO	GC A	TAGA	CGAG	g AC	AAGC	AAGC	CCT	CCGN	ACT							340
(2) INFO	RMAT	ION	FOR S	SEQ :	ID N	D: 2	10:									
(i) SEQUENCE CHARACTERISTICS: (A) LENGTH: 113 amino acids (B) TYPE: amino acid (C) STRANDEDNESS: single (D) TOPOLOGY! linear (ii) MOLECULE TYPE: cDNA																
(ii)	MOL	ECULI	TYI	PE:	CDNA											
(iii) (iii)					0											
(xi)	SEQ	UENCI	E DES	BCRI	PTIO	1: SI	EQ II	on c	21	0:						
Pro 1	Thr	Val	Thr	Glu 5	Arg	Asp	Xaa	Arg	Val 10	Glu	Glu	Glu	Val	Tyr 15	Gln	
Cys	Сув	Asn	Leu 20	Glu	Xaa	Asp	Xaa	Arg 25	Lys	Val	Ile	Asn	Ala 30	Leu	Thr	
Glu	Arg	Leu 35	Tyr	Val	Gly	Gly	Pro 40	Met	His	Asn	Ser	Lys 45	Gly	Asp	Leu	
Сув	Gly 50	Ile	Arg	Arg	Cys	Arg 55	Ala	Ser	Gly	Val	Tyr 60	Thr	Thr	Ser	Phe	
Gly 65	Asn	Thr	Leu	Thr	Cys 70	Tyr	Leu	Lys	Ala	Thr 75	Ala	Ala	Thr	Arg	Ala 80	
Ala	Gly	Leu	Lys	Asp 85	Cys	Thr	Met	Leu	Val 90	Cys	Gly	Asp	Asp	Leu 95	Val	
Val	Ile	Ala	Glu 100	Ser	Ile	Gly	Ile	Asp 105	Glu	Asp	Lys	Gln	Ala 110	Leu	Arg	
Thr																
(2) INFO	RMAT	ION 1	FOR S	SEQ :	ID NO): 2:	11:									
(i) SEQUENCE CHARACTERISTICS: (A) LENGTH: 340 base pairs (B) TYFE: nucleic acid (C) STRANDEDMESS: single (D) TOPOLOGY: linear																

(ii) MOLECULE TYPE: cDNA

HYDOTHETTCAL	

, ,	 ٠.	ANTT-SENSE.	310

(ix) FEATURE:

(A) NAME/KEY: CDS

(B) LOCATION: 1..340

(xi) SEQUENCE DESCRIPTION: SEQ ID NO: 211:

CTCGACTGTG NCCGAGAGGG ACATCAGGAC AGAGGGAGAG GTCTATCAGT GTTGCGACCT 60
GGAACCAGGA GCCGCAAAG TAATCACCGC CCTCACTGAG AGACTCTATG TGGGCGACC 120
CATGTTCAAC AGCAAGGGAG ACCTGTGCGG ACAACGCCGG TGCCGCGCAA GCGGCGTGTT 180
CACCACCAGC TTCGGGAACA CACTGACGTG CTACCTTAAA GCCACAGCTG CTACTAGAGC 240
AGCCGGCTTA AAAGATTGCA CCATGCTGGT CTGCGTGAC GACTTAGTCG TTATTTCCGA 300
GAGCGCCGGT GTGGAGGAGG ATCCCANAAC CCNNCGACCN 340

- (2) INFORMATION FOR SEQ ID NO: 212:
 - (i) SEQUENCE CHARACTERISTICS:
 - (A) LENGTH: 113 amino acids
 - (B) TYPE: amino acid
 - (C) STRANDEDNESS: single
 (D) TOPOLOGY: linear
 - (ii) MOLECULE TYPE: cDNA
 - (iii) HYPOTHETICAL: NO
 - (iii) ANTI-SENSE: NO
 - (xi) SEQUENCE DESCRIPTION: SEQ ID NO: 212:

Ser Thr Val Xaa Glu Arg Asp Ile Arg Thr Glu Gly Glu Val Tyr Gln 1 5 5 10 15

Cys Cys Asp Leu Glu Pro Glu Ala Arg Lys Val Ile Thr Ala Leu Thr

Glu Arg Leu Tyr Val Gly Gly Pro Met Phe Asn Ser Lys Gly Asp Leu $35 \hspace{1cm} 40 \hspace{1cm} 45$

Cys Gly Gln Arg Arg Cys Arg Ala Ser Gly Val Phe Thr Thr Ser Phe 50 55 60

Gly Asn Thr Leu Thr Cys Tyr Leu Lys Ala Thr Ala Ala Thr Arg Ala

267 65 70 75 80 Ala Gly Leu Lys Asp Cys Thr Met Leu Val Cys Gly Asp Asp Leu Val 90 Val Ile Ser Glu Ser Ala Gly Val Glu Glu Asp Pro Xaa Thr Xaa Arq Pro (2) INFORMATION FOR SEQ ID NO: 213: (i) SEQUENCE CHARACTERISTICS: (A) LENGTH: 340 base pairs (B) TYPE: nucleic acid (C) STRANDEDNESS: single (D) TOPOLOGY: linear (ii) MOLECULE TYPE: cDNA (iii) HYPOTHETICAL: NO (iii) ANTI-SENSE: NO (ix) FEATURE: (A) NAME/KEY: CDS (B) LOCATION: 2..340 (ix) FEATURE: (A) NAME/KEY: mat peptide (B) LOCATION: 2..337 (xi) SEQUENCE DESCRIPTION: SEQ ID NO: 213: C TCA ACA GTC ACC GAG AAC GAC ATC CGT GTT GAG GAG TCA ATT TAC Ser Thr Val Thr Glu Asn Asp Ile Arg Val Glu Glu Ser Ile Tyr CAA TGT TGT GAC TTG GCC CCC GAG GCC AGA CAG GCC ATA AAG TCG CTC Gln Cys Cys Asp Leu Ala Pro Glu Ala Arg Gln Ala Ile Lys Ser Leu ACA GAG CGG CTT TAT ATC GGG GGT CCC CTG ACT AAT TCA AAG GGG CAG 142 Thr Glu Arg Leu Tyr Ile Gly Gly Pro Leu Thr Asn Ser Lys Gly Gln AAC TGT GGC TAT CGC CGA TGC CGC GCA AGC GGC GTG CTG ACG ACC AGC 190 Asn Cys Gly Tyr Arg Arg Cys Arg Ala Ser Gly Val Leu Thr Thr Ser 50 TGC GGT AAT ACC CTT ACA TGT TAC"CTA AAG GCC TCT GCA GCC TGT CGA 238 Cys Gly Asn Thr Leu Thr Cys Tyr Leu Lys Ala Ser Ala Ala Cys Arg 70

GCT GCG AAG CTC CAG GAC TGC ACG ATG CTC GTG TGC GGG GAC GAC CTT

Ala Ala Lys Leu Gln Asp Cys Thr Met Leu Val Cys Gly Asp Asp Leu 80 85 90 95

100 105 110

CGA GTC 340 Arg Val

- (2) INFORMATION FOR SEQ ID NO: 214:
 - (i) SEQUENCE CHARACTERISTICS:
 - (A) LENGTH: 113 amino acids
 - (B) TYPE: amino acid (D) TOPOLOGY: linear

 - (ii) MOLECULE TYPE: protein
 - (xi) SEQUENCE DESCRIPTION: SEQ ID NO: 214:

Ser Thr Val Thr Glu Asn Asp Ile Arg Val Glu Glu Ser Ile Tyr Glu 1 15

Cys Cys Asp Leu Ala Pro Glu Ala Arg Gln Ala Ile Lys Ser Leu Thr 20 25 30

Glu Arg Leu Tyr Ile Gly Gly Pro Leu Thr Asn Ser Lys Gly Gln Asn $35 \hspace{1cm} 40 \hspace{1cm} 45$

Cys Gly Tyr Arg Arg Cys Arg Ala Ser Gly Val Leu Thr Thr Ser Cys 50 60

Gly Asn Thr Leu Thr Cys Tyr Leu Lys Ala Ser Ala Ala Cys Arg Ala 65 70 75 80

Ala Lys Leu Gln Asp Cys Thr Met Leu Val Cys Gly Asp Asp Leu Val 85 90 95

Val Ile Cys Glu Ser Ala Gly Thr Gln Glu Asp Ala Ala Ser Leu Arg 100 105 110

Val

- (2) INFORMATION FOR SEQ ID NO: 215:
 - (i) SEQUENCE CHARACTERISTICS:
 - (A) LENGTH: 340 base pairs (B) TYPE: nucleic acid
 - (C) STRANDEDNESS: single
 (D) TOPOLOGY: linear

 - (ii) MOLECULE TYPE: cDNA

(iii) HYPOTHETICAL: NO

	(iii) AN	TI-S	ENSE	: NO										
	(ix	(:	ATUR A) N B) L	AME/											
	(ix	(ATUR A) N B) L	AME/I				tide							
	(xi) SE	QUEN	CE DI	ESCR	IPTI	ON:	SEQ	ID N): 2:	15:				
	CA AG er Ti								rg T				le T		46
	GCT Ala														94
	GAG Glu													CAA Gln	142
	TGC Cys														190
	GGG Gly 65													AAA Lys	238
	GCA Ala														286
	GTC Val		Ser		Ser	Gln	Gly	Asn		Glu					334

(2) INFORMATION FOR SEQ ID NO: 216:

AGA GCT

Arg Ala

- (i) SEQUENCE CHARACTERISTICS:
 - (A) LENGTH: 113 amino acids
 - (B) TYPE: amino acid --(D) TOPOLOGY: linear
- (ii) MOLECULE TYPE: protein

(xi) SEQUENCE DESCRIPTION: SEQ ID NO: 216:

Ser Thr Val Thr Glu Arg Asp Ile Arg Thr Glu Glu Ser Ile Tyr Gln
1 5 10 15

Ala Cys Ser Leu Pro Gln Glu Ala Arg Thr Val Ile His Ser Leu Thr 20 25 30

Glu Arg Leu Tyr Val Gly Gly Pro Met Ile Asn Ser Lys Gly Gln Ser

Cys Gly Tyr Arg Arg Cys Arg Ala Ser Gly Val Phe Thr Thr Ser Met 50 55 60

Gly Asn Thr Met Thr Cys Tyr Ile Lys Ala Leu Ala Ala Cys Lys Ala 65 70 . 75 80

Ala Gly Ile Val Asp Pro Val Met Leu Val Cys Gly Asp Asp Leu Val 85 90 95

Val Ile Ser Glu Ser Gln Gly Asn Glu Glu Asp Glu Arg Asn Leu Arg 100 105 110

Ala

- (2) INFORMATION FOR SEQ ID NO: 217:
 - (i) SEQUENCE CHARACTERISTICS:
 - (A) LENGTH: 340 base pairs
 - (B) TYPE: nucleic acid
 - (C) STRANDEDNESS: single
 (D) TOPOLOGY: linear
 - (ii) MOLECULE TYPE: cDNA
 - (iii) HYPOTHETICAL: NO
 - (iii) ANTI-SENSE: NO
 - (ix) FEATURE:
 - (A) NAME/KEY: CDS
 - (B) LOCATION: 2..340
 - (ix) FEATURE:
 - (A) NAME/KEY: mat_peptide
 - (B) LOCATION: 2..340
 - (xi) SEQUENCE DESCRIPTION: SEQ ID NO: 217:
- C TCG ACT GTC ACT GAA CAG GAC ATC AGG GTG GAA GAG GAG ATA TAT Ser Thr Val Thr Glu Gln Asp Ile Arg Val Glu Glu Glu Ile Tyr 1 5 10 15
- CAA TGC TGC AAC CTT GAA CCG GAG GCC AGG AAA GTG ATC TCC TCC CTC Gln Cys Cys Asn Leu Glu Pro Glu Ala Arg Lys Val Ile Ser Ser Leu

46

20 -25 30 ACG GAG CGG CTT TAC TGC GGA GGC CCT ATG TTT AAC AGC AAG GGG GCC 142 Thr Glu Arg Leu Tyr Cys Gly Gly Pro Met Phe Asn Ser Lys Gly Ala CAG TGT GGT TAT CGC CGT TGC CGT GCC AGT GGA GTT CTG CCT ACC AGC 190 Gln Cys Gly Tyr Arg Arg Cys Arg Ala Ser Gly Val Leu Pro Thr Ser TTT GGC AAC ACA ATC ACT TGT TAC ATC AAG GCC ACA ACG GCC GCG AAG 238 Phe Gly Asn Thr Ile Thr Cys Tyr Ile Lys Ala Thr Thr Ala Ala Lys 70 GCC GCA GGC CTC CGG AAC CCG GAC TTT CTT GTC TGC GGA GAT GAT CTG 286 Ala Ala Gly Leu Arg Asn Pro Asp Phe Leu Val Cys Gly Asp Asp Leu 85 90 GTC GTG GTG GCT GAG AGT GAT GGC GTC GAC GAG GAT AGA GCA GCC CTG 334 Val Val Val Ala Glu Ser Asp Gly Val Asp Glu Asp Arg Ala Ala Leu

340

(2) INFORMATION FOR SEO ID NO: 218:

AGA GCC

Arg Ala

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- (i) SEQUENCE CHARACTERISTICS:
 - (A) LENGTH: 113 amino acids
 - (B) TYPE: amino acid
 - (D) TOPOLOGY: linear
- (ii) MOLECULE TYPE: protein
- (xi) SEQUENCE DESCRIPTION: SEQ ID NO: 218:

Ser Thr Val Thr Glu Gln Asp Ile Arg Val Glu Glu Glu Ile Tyr Gln

Cys Cys Asn Leu Glu Pro Glu Ala Arg Lys Val Ile Ser Ser Leu Thr $20 \hspace{1cm} 25 \hspace{1cm} 30$

Glu Arg Leu Tyr Cys Gly Gly Pro Met Phe Asn Ser Lys Gly Ala Gln
35 40 45

Cys Gly Tyr Arg Arg Cys Arg Ala Ser Gly Val Leu Pro Thr Ser Phe 50 60

Gly Asn Thr Ile Thr Cys Tyr Ile Lys Ala Thr Thr Ala Ala Lys Ala 65 70 75 80

Ala Gly Leu Arg Asn Pro Asp Phe Leu Val Cys Gly Asp Asp Leu Val

Val Val Ala Glu Ser Asp Gly Val Asp Glu Asp Arg Ala Ala Leu Arg 100 105 110 Ala

- (2) INFORMATION FOR SEQ ID NO: 219:
 - (i) SEQUENCE CHARACTERISTICS:
 - (A) LENGTH: 10 amino acids
 - (B) TYPE: amino acid
 - (C) STRANDEDNESS: single
 - (D) TOPOLOGY: linear
 - (ii) MOLECULE TYPE: peptide
 - (xi) SEQUENCE DESCRIPTION: SEQ ID NO: 219:

Arg Ser Glu Gly Arg Thr Ser Trp Ala Gln 1 5 10

- (2) INFORMATION FOR SEQ ID NO: 220:
 - (i) SEQUENCE CHARACTERISTICS:
 - (A) LENGTH: 10 amino acids
 (B) TYPE: amino acid
 - (C) STRANDEDNESS: single
 - (D) TOPOLOGY: linear
 - (ii) MOLECULE TYPE: peptide
 - (xi) SEQUENCE DESCRIPTION: SEQ ID NO: 220:
 - Arg Ser Glu Gly Arg Thr Ser Trp Ala Gln 1 5 10
- (2) INFORMATION FOR SEQ ID NO: 221:
 - (i) SEQUENCE CHARACTERISTICS:
 - (A) LENGTH: 10 amino acids
 - (B) TYPE: amino acid
 - (C) STRANDEDNESS: single (D) TOPOLOGY: linear
 - (ii) MOLECULE TYPE: peptide
 - (xi) SEQUENCE DESCRIPTION: SEQ ID NO: 221:
 - Arg Thr Glu Gly Arg Thr Ser Trp Ala Gln 1 5 10
- (2) INFORMATION FOR SEQ ID NO: 222:
 - (i) SEQUENCE CHARACTERISTICS:(A) LENGTH: 629 base pairs

								-	2/3					
		(c) s	YPE: TRAN OPOL	DEDN	ESS:	sin							
	(ii) MO	LECU	LE T	YPE:	cDN	Ά							
	(iii) ну	POTH	ETIC	AL:	NO								
	(iii) AN	TI-S	ENSE	: NO									
			A) N B) L	AMB/ OCAT										
	,	(A) N					tide						
	(xi) SE	QUEN	CE D	ESCR	IPTI	ON:	SEQ	ID N	0; 2	22:			
								ACT Thr						47
								CAG Gln					CTG Leu	95
													CCA Pro	143
								CTC Leu					CTA Leu	191
		Pro						CGG Arg					GAA Glu	239
								AAA Lys						287
								ACC Thr						335
								TTG Leu 120					ATT Ile	383
			Ile		Leu		Gly	Lys					AAA Lys	431

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GAG	GTG	TTG	TAT	CAA	CAA	TAC	GAT	GAG	ATG	GAA	GAG	TGC	TCA	CAA	GCT	479
Glu	Val	Leu	Tyr	Gln	Gln	Tyr	Asp	Glu	Met	Glu	Glu	Cys	Ser	$_{\tt Gln}$	Ala	
	145					150					155					
	CCA															527
Ala	Pro	Tyr	Ile	Glu	Gln	Ala	Gln	Val	Ile	Ala	His	Gln	Phe	Lys	Glu	
160					165					170					175	
AAA	GTC	CTT	GGA	TTG	CTG	CAG	CGA	GCC	ACC	CAA	CAA	CAA	GCT	GTC	ATT	575
Lys	Val	Leu	Gly	Leu	Leu	Gln	Arg	Ala	Thr	Gln	Gln	Gln	Ala	Val	Ile	
				180					185					190		
GAG	CCC	ATA	GTA	ACT	ACC	AAC	\mathbf{TGG}	CAA	AAG	CTT	GAG	GCC	TTT	TGG	CAC	623
Glu	Pro	Ile	Val	Thr	Thr	Asn	Trp	Gln	Lys	Leu	Glu	Ala	Phe	Trp	His	
			195					200					205			
AAG	CAT															629
Lys	His															

- (2) INFORMATION FOR SEO ID NO: 223:
 - (i) SEQUENCE CHARACTERISTICS:
 - (A) LENGTH: 209 amino acids
 - (B) TYPE: amino acid (D) TOPOLOGY: linear
 - (ii) MOLECULE TYPE: protein
 - (xi) SEQUENCE DESCRIPTION: SEQ ID NO: 223:

Asp Phe Trp Glu Ser Val Phe Thr Gly Leu Thr His Ile Asp Ala His 1 $$ 10 $$ 15

Phe Leu Ser Gln Thr Lys Gln Gln Gly Leu Asn Phe Ser Phe Leu Thr

Ala Tyr Gln Ala Thr Val Cys Ala Arg Ala Gln Ala Pro Pro Pro Ser

Trp Asp Glu Met Trp Lys Cys Leu Val Arg Leu Lys Pro Thr Leu His

Gly Pro Thr Pro Leu Leu Tyr Arg Leu Gly Pro Val Gln Asn Glu Ile 65 70 75 80

Cys Leu Thr His Pro Ile Thr Lys Tyr Ile Met Ala Cys Met Ser Ala 85 90 95

Asp Leu Glu Val Thr Thr Ser Thr Trp Val Leu Leu Gly Gly Val Leu
100 105 110

Ala Ala Leu Ala Ala Tyr Cys Leu Ser Val Gly Cys Val Val Ile Val 115 120 125

Gly His Ile Glu Leu Gly Gly Lys Pro Ala Ile Val Pro Asp Lys Glu 130 135 140 Val Leu Tyr Gln Gln Tyr Asp Glu Met Glu Glu Cys Ser Gln Ala Ala 145 150 150 160

Pro Tyr Ile Glu Gln Ala Gln Val Ile Ala His Gln Phe Lys Glu Lys 165 170 175

Val Leu Gly Leu Leu Gln Arg Ala Thr Gln Gln Gln Ala Val Ile Glu 180 185 190

Pro Ile Val Thr Thr Asn Trp Gln Lys Leu Glu Ala Phe Trp His Lys 195 200 205

His

- (2) INFORMATION FOR SEO ID NO: 224:
 - (i) SEQUENCE CHARACTERISTICS:
 - (A) LENGTH: 12 amino acids
 - (B) TYPE: amino acid
 - (C) STRANDEDNESS: single
 (D) TOPOLOGY: linear
 - (ii) MOLECULE TYPE: peptide
 - (ix) FEATURE:
 - (A) NAME/KEY: Peptide
 - (B) LOCATION: 2..12
 - (xi) SEQUENCE DESCRIPTION: SEQ ID NO: 224:

Ile His Tyr Arg Asn Ala Ser Gly Ile Tyr His Ile
1 5 10

- (2) INFORMATION FOR SEQ ID NO: 225:
 - (i) SEQUENCE CHARACTERISTICS:
 - (A) LENGTH: 12 amino acids
 - (B) TYPE: amino acid (C) STRANDEDNESS: single
 - (D) TOPOLOGY: linear
 - (ii) MOLECULE TYPE: peptide

 - (xi) SEQUENCE DESCRIPTION: SEQ ID NO: 225:

Val Asn Tyr Arg Asn Ala Ser Gly Ile Tyr His Ile 1 5 " 1:

- (2) INFORMATION FOR SEQ ID NO: 5:
 - (i) SEQUENCE CHARACTERISTICS:

- (A) LENGTH: 12 amino acids
- (B) TYPE: amino acid
- (C) STRANDEDNESS: single
- (D) TOPOLOGY: linear
- (ii) MOLECULE TYPE: peptide
- (xi) SEQUENCE DESCRIPTION: SEQ ID NO: 226:
- Val Asn Tyr Arg Asn Ala Ser Gly Val Tyr His Ile
- (2) INFORMATION FOR SEO ID NO: 227:
 - (i) SEQUENCE CHARACTERISTICS:
 - (A) LENGTH: 12 amino acids
 - (B) TYPE: amino acid
 - (C) STRANDEDNESS: single
 - (D) TOPOLOGY: linear
 - (ii) MOLECULE TYPE: peptide
 - (xi) SEQUENCE DESCRIPTION: SEQ ID NO: 227:
 - Val Asn Tyr His Asn Thr Ser Gly Ile Tyr His Leu 1 $$ 5
- (2) INFORMATION FOR SEQ ID NO: 228:
 - (i) SEQUENCE CHARACTERISTICS:
 - (A) LENGTH: 12 amino acids
 - (B) TYPE: amino acid
 - (C) STRANDEDNESS: single (D) TOPOLOGY: linear
 - (ii) MOLECULE TYPE: peptide
 - (xi) SEQUENCE DESCRIPTION: SEQ ID NO: 228:
 - Gln His Tyr Arg Asn Ala Ser Gly Ile Tyr His Val
- (2) INFORMATION FOR SEQ ID NO: 229:
 - (i) SEQUENCE CHARACTERISTICS:
 - (A) LENGTH: 12 amino acids
 - (B) TYPE: amino acid
 - (C) STRANDEDNESS: single
 - (D) TOPOLOGY: linear
 - (ii) MOLECULE TYPE: peptide

(xi) SEQUENCE DESCRIPTION: SEQ ID NO: 229:

Gln His Tyr Arg Asn Val Ser Gly Ile Tyr His Val 1 5 10

- (2) INFORMATION FOR SEQ ID NO: 230:
 - (i) SEQUENCE CHARACTERISTICS:
 - (A) LENGTH: 12 amino acids
 - (B) TYPE: amino acid
 - (C) STRANDEDNESS: single
 - (D) TOPOLOGY: linear
 - (ii) MOLECULE TYPE: peptide
 - (xi) SEQUENCE DESCRIPTION: SEQ ID NO: 230:

Ile His Tyr Arg Asn Ala Ser Asp Gly Tyr Tyr Ile 1 5 10

- (2) INFORMATION FOR SEQ ID NO: 231:
 - (i) SEQUENCE CHARACTERISTICS:
 - (A) LENGTH: 12 amino acids
 - (B) TYPE: amino acid (C) STRANDEDNESS: single
 - (D) TOPOLOGY: linear
 - (ii) MOLECULE TYPE: peptide
 - (xi) SEQUENCE DESCRIPTION: SEQ ID NO: 231:

Leu Gln Val Lys Asn Thr Ser Ser Ser Tyr Met Val

- (2) INFORMATION FOR SEO ID NO: 232:
 - (i) SEQUENCE CHARACTERISTICS:
 - (A) LENGTH: 11 amino acids
 - (B) TYPE: amino acid
 - (C) STRANDEDNESS: single
 - (D) TOPOLOGY: linear
 - (ii) MOLECULE TYPE: peptide
 - (xi) SEQUENCE DESCRIPTION: SEQ ID NO: 232:

Val Trp Gln Leu Arg Ala Ile Val Leu His Val

(2) INFORMATION FOR SEQ ID NO: 233:

- (i) SEQUENCE CHARACTERISTICS:
 - (A) LENGTH: 11 amino acids
 - (B) TYPE: amino acid
 - (C) STRANDEDNESS: single (D) TOPOLOGY: linear
- (ii) MOLECULE TYPE: peptide
- (xi) SEQUENCE DESCRIPTION: SEQ ID NO: 233:
- Val Tyr Glu Ala Asp Tyr His Ile Leu His Leu
- (2) INFORMATION FOR SEQ ID NO: 234:
 - (i) SEQUENCE CHARACTERISTICS:
 - (A) LENGTH: 11 amino acids
 - (B) TYPE: amino acid
 - (C) STRANDEDNESS: single (D) TOPOLOGY: linear
 - (ii) MOLECULE TYPE: peptide
 - (xi) SEQUENCE DESCRIPTION: SEQ ID NO: 234:
 - Val Tvr Glu Thr Asp Asn His Ile Leu His Leu
- (2) INFORMATION FOR SEQ ID NO: 235:
 - (i) SEQUENCE CHARACTERISTICS:
 - (A) LENGTH: 11 amino acids (C) STRANDEDNESS: single
 - (B) TYPE: amino acid
 - (D) TOPOLOGY: linear
 - (ii) MOLECULE TYPE: peptide
 - (x1) SECUENCE DESCRIPTION: SEC ID NO: 235:
 - Val Tyr Glu Thr Glu Asn His Ile Leu His Leu
- (2) INFORMATION FOR SEQ ID NO: 236:
 - (i) SEQUENCE CHARACTERISTICS:
 - (A) LENGTH: 11 amino acids (B) TYPE: amino acid "
 - (C) STRANDEDNESS: single
 - (D) TOPOLOGY: linear

 - (ii) MOLECULE TYPE: peptide

- (xi) SEQUENCE DESCRIPTION: SEQ ID NO: 236:
- Val Phe Glu Thr Val His His Ile Leu His Leu 1 5 10
- (2) INFORMATION FOR SEQ ID NO: 237:
 - (i) SEQUENCE CHARACTERISTICS:
 - (A) LENGTH: 11 amino acids
 - (B) TYPE: amino acid
 - (C) STRANDEDNESS: single (D) TOPOLOGY: linear
 - (ii) MOLECULE TYPE: peptide
 - (xi) SEQUENCE DESCRIPTION: SEQ ID NO: 237:
 - Val Phe Glu Thr Glu His His Ile Leu His Leu 1 5 10
- (2) INFORMATION FOR SEQ ID NO: 238:
 - (i) SEQUENCE CHARACTERISTICS:
 - (A) LENGTH: 11 amino acids
 - (B) TYPE: amino acid
 - (C) STRANDEDNESS: single
 (D) TOPOLOGY: linear
 - (ii) MOLECULE TYPE: peptide
 - (xi) SEQUENCE DESCRIPTION: SEQ ID NO: 238:
 - Val Phe Glu Thr Asp His His Ile Met His Leu
- (2) INFORMATION FOR SEQ ID NO: 239:
 - (i) SEQUENCE CHARACTERISTICS:
 - (A) LENGTH: 11 amino acids
 - (B) TYPE: amino acid
 - (C) STRANDEDNESS: single
 - (D) TOPOLOGY: linear
 - (ii) MOLECULE TYPE: peptide
 - (xi) SEQUENCE DESCRIPTION: SEQ ID NO: 239:
 - Val Tyr Glu Thr Glu Asn His Ile Leu His Leu

- (2) INFORMATION FOR SEC ID NO: 240:
 - (i) SEQUENCE CHARACTERISTICS:
 - (A) LENGTH: 11 amino acids
 - (B) TYPE: amino acid
 - (C) STRANDEDNESS: single
 - (D) TOPOLOGY: linear
 - (ii) MOLECULE TYPE: peptide
 - (xi) SEQUENCE DESCRIPTION: SEQ ID NO: 240:

Val Tyr Glu Ala Asp Ala Leu Ile Leu His Ala 5

- (2) INFORMATION FOR SEO ID NO: 241:
 - (i) SEQUENCE CHARACTERISTICS:
 - (A) LENGTH: 13 amino acids
 - (B) TYPE: amino acid (C) STRANDEDNESS: single
 - (D) TOPOLOGY: linear
 - (ii) MOLECULE TYPE: peptide
 - (xi) SEQUENCE DESCRIPTION: SEQ ID NO: 241:

Val Gln Asp Gly Asn Thr Ser Ala Cys Trp Thr Pro Val

- (2) INFORMATION FOR SEO ID NO: 242:
 - (i) SEQUENCE CHARACTERISTICS:
 - (A) LENGTH: 13 amino acids
 - (B) TYPE: amino acid
 - (C) STRANDEDNESS: single (D) TOPOLOGY: linear
 - (ii) MOLECULE TYPE: peptide

 - (xi) SEQUENCE DESCRIPTION: SEQ ID NO: 242: Val Lys Thr Gly Asn Gln Ser Arg Cys Trp Val Ala Leu

1 5 10

- (2) INFORMATION FOR SEQ ID NO: 243:
 - (i) SEQUENCE CHARACTERISTICS:
 - (A) LENGTH: 13 amino acids
 - (B) TYPE: amino acid
 - (C) STRANDEDNESS: single
 - (D) TOPOLOGY: linear

- (ii) MOLECULE TYPE: peptide
- (xi) SEQUENCE DESCRIPTION: SEQ ID NO: 243:

Val Lys Thr Gly Asn Gln Ser Arg Cys Trp Val Ala Leu

- (2) INFORMATION FOR SEO ID NO: 244:
 - (i) SEQUENCE CHARACTERISTICS:
 - (A) LENGTH: 13 amino acids
 - (B) TYPE: amino acid
 - (C) STRANDEDNESS: single
 - (D) TOPOLOGY: linear
 - (ii) MOLECULE TYPE: peptide
 - (xi) SEQUENCE DESCRIPTION: SEQ ID NO: 244:

Val Arg Thr Gly Asn Gln Ser Arg Cys Trp Val Ala Leu 1 5 10

- (2) INFORMATION FOR SEQ ID NO: 245:
 - (i) SEOUENCE CHARACTERISTICS:
 - (A) LENGTH: 13 amino acids
 - (B) TYPE: amino acid
 - (C) STRANDEDNESS: single
 (D) TOPOLOGY: linear
 - (ii) MOLECULE TYPE: peptide
 - (xi) SEQUENCE DESCRIPTION: SEQ ID NO: 245:

Val Lys Thr Gly Asn Gln Ser Arg Cys Trp Ile Ala Leu

- (2) INFORMATION FOR SEQ ID NO: 246:
 - (i) SEQUENCE CHARACTERISTICS:
 - (A) LENGTH: 13 amino acids
 - (B) TYPE: amino acid
 - (C) STRANDEDNESS: single
 (D) TOPOLOGY: linear
 - (ii) MOLECULE TYPE: peptide
 - (xi) SEQUENCE DESCRIPTION: SEQ ID NO: 246:

Val Lys Thr Gly Asn Gln Ser Arg Cys Trp Ile Ala Leu

:

5 10

- (2) INFORMATION FOR SEO ID NO: 247:
 - (i) SEQUENCE CHARACTERISTICS:
 - (A) LENGTH: 13 amino acids
 - (B) TYPE: amino acid (C) STRANDEDNESS: single
 - (C) STRANDEDNESS: SINGLE (D) TOPOLOGY: linear
 - (ii) MOLECULE TYPE: peptide

 - (xi) SEQUENCE DESCRIPTION: SEQ ID NO: 247:

Val Lys Thr Gly Asn Ser Val Arg Cys Trp Ile Pro Leu 1 5 10

- (2) INFORMATION FOR SEQ ID NO: 248:
 - (i) SEQUENCE CHARACTERISTICS:
 - (A) LENGTH: 13 amino acids
 - (B) TYPE: amino acid
 - (C) STRANDEDNESS: single
 (D) TOPOLOGY: linear
 - (ii) MOLECULE TYPE: peptide
 - (xi) SEQUENCE DESCRIPTION: SEO ID NO: 248:

Val Lys Thr Gly Asn Val Ser Arg Cys Trp Ile Ser Leu

- (2) INFORMATION FOR SEQ ID NO: 249:
 - (i) SEQUENCE CHARACTERISTICS:
 - (A) LENGTH: 13 amino acids
 - (B) TYPE: amino acid
 - (C) STRANDEDNESS: single
 - (D) TOPOLOGY: linear
 - (ii) MOLECULE TYPE: peptide
 - (xi) SEQUENCE DESCRIPTION: SEQ ID NO: 249:

Val Arg Lys Asp Asn Val Ser Arg Cys Trp Val Gln Ile

- (2) INFORMATION FOR SEO ID NO: 250:
 - (i) SEQUENCE CHARACTERISTICS:
 - (A) LENGTH: 10 amino acids
 - (B) TYPE: amino acid

- (C) STRANDEDNESS: single
- (D) TOPOLOGY: linear
- (ii) MOLECULE TYPE: peptide
- (xi) SEQUENCE DESCRIPTION: SEQ ID NO: 250:
- Ala Pro Ser Phe Gly Ala Val Thr Ala Pro
- (2) INFORMATION FOR SEQ ID NO: 251:
 - (i) SEQUENCE CHARACTERISTICS:
 - (A) LENGTH: 10 amino acids
 - (B) TYPE: amino acid
 - (C) STRANDEDNESS: single
 - (D) TOPOLOGY: linear
 - (ii) MOLECULE TYPE: peptide
 - (xi) SEQUENCE DESCRIPTION: SEO ID NO: 251:
 - Val Ser Gln Pro Gly Ala Leu Thr Lys Gly
- (2) INFORMATION FOR SEO ID NO: 252:
 - (i) SEQUENCE CHARACTERISTICS:
 - (A) LENGTH: 10 amino acids
 - (B) TYPE: amino acid
 - (C) STRANDEDNESS: single
 - (D) TOPOLOGY: linear
 - (ii) MOLECULE TYPE: peptide
 - (xi) SEQUENCE DESCRIPTION: SEO ID NO: 252:
 - Val Lys Tyr Val Gly Ala Thr Thr Ala Ser 1 5 10
- (2) INFORMATION FOR SEQ ID NO: 253:
 - (i) SEQUENCE CHARACTERISTICS:
 - (A) LENGTH: 10 amino acids
 - (B) TYPE: amino acid
 - (C) STRANDEDNESS: single
 - (D) TOPOLOGY: linear
 - (ii) MOLECULE TYPE: peptide
 - (xi) SEQUENCE DESCRIPTION: SEQ ID NO: 253:

Ala Pro Tyr Ile Gly Ala Pro Val Glu Ser

- (2) INFORMATION FOR SEQ ID NO: 254:
 - (i) SECUENCE CHARACTERISTICS:
 - (A) LENGTH: 10 amino acids

 - (B) TYPE: amino acid
 - (C) STRANDEDNESS: single (D) TOPOLOGY: linear
 - (ii) MOLECULE TYPE: peptide
 - (xi) SEQUENCE DESCRIPTION: SEQ ID NO: 254:

Ala Gln His Leu Asn Ala Pro Leu Glu Ser 5

- (2) INFORMATION FOR SEQ ID NO: 255:
 - (i) SEQUENCE CHARACTERISTICS:
 - (A) LENGTH: 10 amino acids
 - (B) TYPE: amino acid
 - (C) STRANDEDNESS: single (D) TOPOLOGY: linear
 - (ii) MOLECULE TYPE: peptide
 - (xi) SEQUENCE DESCRIPTION: SEO ID NO: 255:

Ser Pro Tyr Val Gly Ala Pro Leu Glu Pro

- (2) INFORMATION FOR SEO ID NO: 256:
 - (i) SEQUENCE CHARACTERISTICS:
 - (A) LENGTH: 10 amino acids
 - (B) TYPE: amino acid
 - (C) STRANDEDNESS: single
 - (D) TOPOLOGY: linear
 - (ii) MOLECULE TYPE: peptide
- (xi) SEQUENCE DESCRIPTION: SEQ ID NO: 256:

Ser Pro Tyr Ala Gly Ala Pro Leu Glu Pro 5

- (2) INFORMATION FOR SEQ ID NO: 257:
 - (i) SEQUENCE CHARACTERISTICS: (A) LENGTH: 10 amino acids

- (B) TYPE: amino acid
- (C) STRANDEDNESS: single
- (C) STRANDEDNESS: SINGLE (D) TOPOLOGY: linear
- (ii) MOLECULE TYPE: peptide
- (xi) SEQUENCE DESCRIPTION: SEQ ID NO: 257:

Ala Pro Tyr Leu Gly Ala Pro Leu Glu Ser

- (2) INFORMATION FOR SEQ ID NO: 258:
 - (i) SEQUENCE CHARACTERISTICS:
 - (A) LENGTH: 10 amino acids
 - (B) TYPE: amino acid
 - (C) STRANDEDNESS: single (D) TOPOLOGY: linear
 - (ii) MOLECULE TYPE: peptide
 - (xi) SEQUENCE DESCRIPTION: SEQ ID NO: 258:

Ala Pro Tyr Leu Gly Ala Pro Leu Glu Ser 1 5 10

- (2) INFORMATION FOR SEO ID NO: 259:
 - (i) SEQUENCE CHARACTERISTICS:
 - (A) LENGTH: 10 amino acids
 - (B) TYPE: amino acid
 - (C) STRANDEDNESS: single
 - (D) TOPOLOGY: linear
 - (ii) MOLECULE TYPE: peptide
 - (xi) SEQUENCE DESCRIPTION: SEQ ID NO: 259:

Ala Pro Tyr Val Gly Ala Pro Leu Glu Ser 1 5 10

- (2) INFORMATION FOR SEQ ID NO: 260:
 - (i) SEQUENCE CHARACTERISTICS:
 - (A) LENGTH: 11 amino acids
 - (B) TYPE: amino acid
 - (C) STRANDEDNESS: single
 - (D) TOPOLOGY: linear
 - (ii) MOLECULE TYPE: peptide

:

(xi) SEQUENCE DESCRIPTION: SEQ ID NO: 260:

Asn Val Pro Tyr Leu Gly Ala Pro Leu Thr Ser 1 5 10

- (2) INFORMATION FOR SEQ ID NO: 261:
 - (i) SEQUENCE CHARACTERISTICS:
 - (A) LENGTH: 10 amino acids
 - (B) TYPE: amino acid
 - (C) STRANDEDNESS: single
 - (D) TOPOLOGY: linear
 - (ii) MOLECULE TYPE: peptide
 - (xi) SEQUENCE DESCRIPTION: SEQ ID NO: 261:

Ala Pro His Leu Arg Ala Pro Leu Ser Ser 1 5 10

- (2) INFORMATION FOR SEQ ID NO: 262:
 - (i) SEQUENCE CHARACTERISTICS:
 - (A) LENGTH: 10 amino acids
 - (B) TYPE: amino acid
 - (C) STRANDEDNESS: single
 (D) TOPOLOGY: linear
 - (ii) MOLECULE TYPE: peptide
 - (xi) SEQUENCE DESCRIPTION: SEO ID NO: 262:

Ala Pro Tyr Leu Gly Ala Pro Leu Thr Ser 1 5 10

- (2) INFORMATION FOR SEQ ID NO: 263:
 - (i) SEQUENCE CHARACTERISTICS:
 - (A) LENGTH: 10 amino acids
 - (B) TYPE: amino acid
 - (C) STRANDEDNESS: single
 - (D) TOPOLOGY: linear
 - (ii) MOLECULE TYPE: peptide
 - (xi) SEQUENCE DESCRIPTION: SEQ ID NO: 263:

Arg Pro Arg Gln His Ala Thr Val Gln Asp 1 5 10

(2) INFORMATION FOR SEQ ID NO: 264:

- (i) SEQUENCE CHARACTERISTICS:
 - (A) LENGTH: 10 amino acids
 - (B) TYPE: amino acid
 - (C) STRANDEDNESS: single
- (D) TOPOLOGY: linear
- (ii) MOLECULE TYPE: peptide
- (xi) SEQUENCE DESCRIPTION: SEQ ID NO: 264:

Ser Pro Gln His His Lys Phe Val Gln Asp 1 5 10

- (2) INFORMATION FOR SEQ ID NO: 265:
 - (i) SEQUENCE CHARACTERISTICS:
 - (A) LENGTH: 10 amino acids
 - (B) TYPE: amino acid
 (C) STRANDEDNESS: single
 - (D) TOPOLOGY: linear
 - (ii) MOLECULE TYPE: peptide
 - (xi) SEQUENCE DESCRIPTION: SEQ ID NO: 265:

- (2) INFORMATION FOR SEO ID NO: 266:
 - (i) SEQUENCE CHARACTERISTICS:
 - (A) LENGTH: 10 amino acids
 - (B) TYPE: amino acid
 - (C) STRANDEDNESS: single
 - (D) TOPOLOGY: linear
 - (ii) MOLECULE TYPE: peptide
 - (xi) SEQUENCE DESCRIPTION: SEQ ID NO: 266:

Pro Pro Arg Ile His Glu Thr Thr Gln Asp 1 5 10

- (2) INFORMATION FOR SEQ ID NO: 267:
 - (i) SEQUENCE CHARACTERISTICS:
 - (A) LENGTH: 14 amino acids
 - (B) TYPE: amino acid
 - (C) STRANDEDNESS: single
 - (D) TOPOLOGY: linear

- (ii) MOLECULE TYPE: peptide
- (xi) SEQUENCE DESCRIPTION: SEQ ID NO: 267:

Thr Ile Ser Tyr Ala Asn Gly Ser Gly Pro Ser Asp Asp Lys

- (2) INFORMATION FOR SEQ ID NO: 268:
 - (i) SEQUENCE CHARACTERISTICS:
 - (A) LENGTH: 19 amino acids
 - (B) TYPE: amino acid
 - (C) STRANDEDNESS: single
 - (D) TOPOLOGY: linear
 - (ii) MOLECULE TYPE: peptide
 - (xi) SEQUENCE DESCRIPTION: SEQ ID NO: 268:

Trp Ala Gln

- (2) INFORMATION FOR SEQ ID NO: 269:
 - (i) SEQUENCE CHARACTERISTICS:
 - (A) LENGTH: 1443 base pairs
 - (B) TYPE: nucleic acid
 - (C) STRANDEDNESS: single (D) TOPOLOGY: linear
 - (ii) MOLECULE TYPE: DNA (genomic)
 - (iii) HYPOTHETICAL: NO
 - (iii) ANTI-SENSE: NO
 - (ix) FEATURE:
 - (A) NAME/KEY: CDS
 - (B) LOCATION: 1..1443
 - (ix) FEATURE:
 - (A) NAME/KEY: mat_peptide
 - (B) LOCATION: 1..1443
 - (xi) SEQUENCE DESCRIPTION: SEQ ID NO: 269:

ACC ATC ACC ACC GGA GCT TCT ATC ACA TAC TCC ACT TAC GGC AAG TTC Thr Ile Thr Thr Gly Ala Ser Ile Thr Tyr Ser Thr Tyr Gly Lys Phe $\,$

WO 94/25601 PCT/EP94/01323 289 15 CTT GCT GAT GGA GGG TGT TCA GGC GGC GCG TAT GAC GTG ATC ATA TGC 96 Leu Ala Asp Gly Gly Cys Ser Gly Gly Ala Tyr Asp Val Ile Ile Cys 20 GAC GAG TGC CAT TCC CAG GAC GCC ACC ACC ATT CTT GGG ATA GGC ACT Asp Glu Cys His Ser Gln Asp Ala Thr Thr Ile Leu Gly Ile Gly Thr GTC CTT GAC CAG GCA GAG ACG GCT GGA GCT AGG CTC GTC GTC TTG GCC 192 Val Leu Asp Gln Ala Glu Thr Ala Gly Ala Arg Leu Val Val Leu Ala ACG GCC ACC CCT CCC GGC AGT GTG ACA ACG CCC CAC CCC AAC ATC GAG 240 Thr Ala Thr Pro Pro Gly Ser Val Thr Thr Pro His Pro Asn Ile Glu GAA GTG GCC CTG CCT CAG GAG GGG GAG GTT CCC TTC TAC GGC AGA GCC 288 Glu Val Ala Leu Pro Gln Glu Gly Glu Val Pro Phe Tyr Gly Arg Ala ATT CCC CTT GCT TTT ATA AAG GGT GGT AGG CAT CTC ATC TTC TGC CAT 336 Ile Pro Leu Ala Phe Ile Lys Gly Gly Arg His Leu Ile Phe Cys His TCC AAG AAA AAA TGT GAT GAA CTC GCC AAG CAA CTG ACC AGC CTG GGC Ser Lys Lys Cys Asp Glu Leu Ala Lys Gln Leu Thr Ser Leu Gly 115 120 GTG AAC GCC GTG GCA TAT TAT AGA GGT CTA GAC GTC GCC GTC ATC CCC 432 Val Asn Ala Val Ala Tyr Tyr Arg Gly Leu Asp Val Ala Val Ile Pro 130 135 ACA GCA GGA GAC GTG GTC GTG TGC AGC ACC GAC GCG CTC ATG ACG GGA Thr Ala Gly Asp Val Val Val Cys Ser Thr Asp Ala Leu Met Thr Gly 145 TTC ACC GGC GAC TTT GAT TCT GTC ATA GAC TGC AAC TCC GCC GTC ACT 528 Phe Thr Gly Asp Phe Asp Ser Val Ile Asp Cys Asn Ser Ala Val Thr 165

ACA GTG CCC CAG GAC GCA GTG TCC AGA AGC CAG CGT AGG GGC GGC ACG
Thr Val Pro Gln Asp Ala Val Ser Arg Ser Gln Arg Arg Gly Arg Thr
195
200
GGG AGA GGT AGG CAC GGC ATA TAC CGG TAT GTC TCG GCT GGA GAG AGA
Gly Arg Gly Arg His Gly Ile Tyr Arg Tyr Val Ser Ala Gly Glu Arg
210
215
226
662
672
673

576

CAG ACG GTG GAC TTC AGT CTG GAT CCC ACT TTT ACC ATT GAG ACT ACC

Gln Thr Val Asp Phe Ser Leu Asp Pro Thr Phe Thr Ile Glu Thr Thr

180

CCS TCT GAC ATS TTC GAC TCC GTG GTG CTC TGT GAG TGC TAC GAT GCC
Pro Ser Asp Met Phe Asp Ser Val Val Leu Cys Glu Cys Tyr Asp Ala
225 230 240

110 94	2300.					29	n			CIII	4/01525
				GAT Asp		CCT	GCC			TTG Leu	768
				ACC Thr							816
				GTG Val							864
				AAA Lys							912
				GTC Val 310							960
				AAA Lys							1008
				TTG Leu							1056
				ATC Ile							1104
				ACC Thr							1152
				TAC Tyr 390							1200
				TCT Ser							1248
				TTT Phe							1296
				ACA Thr							1344
				AGC Ser						AAG Lys	1392
		Ala		GTG Val 470							1440

TAC Tyr 1443

- (2) INFORMATION FOR SEQ ID NO: 270:
 - (i) SEQUENCE CHARACTERISTICS:
 - (A) LENGTH: 481 amino acids
 - (B) TYPE: amino acid
 - (D) TOPOLOGY: linear
 - (ii) MOLECULE TYPE: protein
 - (xi) SEQUENCE DESCRIPTION: SEQ ID NO: 270:

Thr Ile Thr Thr Gly Ala Ser Ile Thr Tyr Ser Thr Tyr Gly Lys Phe
1 5 10 15

Leu Ala Asp Gly Gly Cys Ser Gly Gly Ala Tyr Asp Val Ile Ile Cys 20 25 30

Asp Glu Cys His Ser Gln Asp Ala Thr Thr Ile Leu Gly Ile Gly Thr . 35 40 45

Val Leu Asp Gln Ala Glu Thr Ala Gly Ala Arg Leu Val Val Leu Ala 50 60

Ile Pro Leu Ala Phe Ile Lys Gly Gly Arg His Leu Ile Phe Cys His

Ser Lys Lys Cys Asp Glu Leu Ala Lys Gln Leu Thr Ser Leu Gly 115 120 125

Val Asn Ala Val Ala Tyr Tyr Arg Gly Leu Asp Val Ala Val Ile Pro 130 135 140

Thr Ala Gly Asp Val Val Cys Ser Thr Asp Ala Leu Met Thr Gly 145 150 155 160

Phe Thr Gly Asp Phe Asp Ser Val Ile Asp Cys Asn Ser Ala Val Thr 165 170 175

Gln Thr Val Asp Phe Ser Leu Asp Pro Thr Phe Thr Ile Glu Thr Thr

Thr Val Pro Gln Asp Ala Val Ser Arg Ser Gln Arg Arg Gly Arg Thr

Gly Arg Gly Arg His Gly Ile Tyr Arg Tyr Val Ser Ala Gly Glu Arg 210 215 220

Pro Ser Asp Met Phe Asp Ser Val Val Leu Cys Glu Cys Tyr Asp Ala

292 225 230 235 Gly Cys Ala Trp Tyr Asp Leu Thr Pro Ala Glu Thr Thr Val Arg Leu 250 Arg Ala Tyr Ile Asn Thr Pro Gly Leu Pro Val Cys Gln Asp His Leu 265 Glu Phe Trp Glu Gly Val Phe Thr Gly Leu Thr Asn Ile Asp Ala His Met Leu Ser Gln Thr Lys Gln Gly Gly Glu Asn Phe Pro Tyr Leu Val Ala Tyr Gln Ala Thr Val Cys Val Arg Ala Lys Ala Pro Pro Pro Ser 305 Trp Asp Thr Met Trp Lys Cys Met Leu Arg Leu Lys Pro Thr Leu Thr 330 Gly Pro Thr Pro Leu Leu Tyr Arg Leu Gly Pro Val Gln Asn Glu Ile Thr Leu Thr His Pro Ile Thr Lys Tyr Ile Met Ala Cys Met Ser Ala Asp Leu Glu Val Ile Thr Ser Thr Trp Val Leu Val Gly Gly Val Val 375

Ala Ala Leu Ala Ala Tyr Cys Leu Thr Val Gly Ser Val Ala Ile Val 385 390 400

Gly Arg Ile Ile Leu Ser Gly Lys Pro Ala Ile Ile Pro Asp Arg Glu
405 410 415

Ala Leu Tyr Gln Gln Phe Asp Glu Met Glu Glu Cys Ser Ala Ser Leu 420 425 430

Pro Tyr Met Asp Glu Thr Arg Ala Ile Ala Gly Gln Phe Lys Glu Lys 435 440 445

Val Leu Gly Phe Ile Ser Thr Thr Gly Gln Lys Ala Glu Thr Leu Lys 450 455

Pro Ala Ala Thr Ser Val Trp Asn Lys Ala Glu Gln Phe Trp Ala Thr 465 470 480

Tyr

1/111
CTCCACAGTCACTGAGAGCGACATCCGTACGGAGGAGGCAATCTACCAAT AG
28284 4 4 4 4 4 4 4 4 4 4 4 4 4 4 4 4 4
79373 1.1
33993333333333333333333333333333333333
HCV-1 HCV-1 BEG00 2TY4 4TY4 4TY4 HC-48 HC-48 NE91 NE91 ARG6 NE92 ARG6 NE92 ARG6 NE92 ARG8 NE92 ARG8 NE92 ARG8 NE92 ARG8 NE92 ARG8 NE92 ARG8 NE92 ARG8 NE92 ARG8 NE92 ARG8 NE92 ARG8 NE92 ARG8 NE92 ARG8 NE92 ARG8 NE92 ARG8 NE92 ARG8 NE92 ARG8 NE92 ARG8 ARG8 ARG8 ARG8 ARG8 ARG8 ARG8 ARG8

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- T
Figure

7932	TACA-AGA-GGTCAGGTG	TACA-AGA-GGTCAGG-ATG	TACA-AAA-GGTCAGG-ATG	TACA-AGA-GGTCAGG-G-TG	TGAAAGGTCAA-GTG	TGTGTGGTCAA-A-GT	A-GG	GGCAGTA-GCA-AGG	A-AGG	-CCGNGNA-GGTCA-AGGTG	GTGN-CGA-GAGA-AGGTG	0L9	5L5	GCTCACATAATGCAT-CT	AC-C-C-ACATATTGTAT-CA	GCTCACATAATGTAT-TT	GTCACATAATGTAT-CT	
																•		
	4 C	4°C	4 C	4 0	4e	4e	4 £	49	4 h	41	4.	4k	4k	Бa	5a	ъ В	ದ	
	GB48	GB116	GB215	GB358	GB809	CAM600	CAMG22	GB549	S GB438	S CAR4/1205	<pre>GAR1/501</pre>	III EG-13	S EG-19	BE95) I BE96	CHR18	E CHR19)

D 7982 8031	GITGTGACCTCGACCCCCAAGCCCGCGTGGCCATCAAGTCCCTCACCGAG	G-CA-9-G-G	GCG-C		CTC-T-GCC-GAGG-GA-ACTAC-CAGT	CTCTGCCT-AAGA-AACT-TAC-CGT	CTCGCCAAG-GA-AACT-TAC-CG	CTCGCCT-AAG-GA-AACT-TAC-CGT	CCTCAGCCTGAGG-GTAACTAC-CAGT	CCTCAGCC-GAGG-GTAACTTAC-CAGT	CCCTCAGCCTGAGG-GAACTTAC-CAGT	CTCAGCCT-AGG-GTGACTTAC-CAT-GT	CCTCTT-ACC-GAGGAGACTAC-CAG-	AGG-GA-GAAA-TG	AGG-GA-GAAA-TGTCC	-CATAGG-GA-GAAA-TGTCCGA	-CATAGG-GA-GAGA-TGTCCG	TGGG-GA-GAAA-TG	-CCATAGG-GA-GAAA-TGTCCG	.ATAGG-G	-CATAGG-GA-GAAA-TGTCCG	-CATAGG-GA-GAAA-TGTCCGA	-CATAGG-GA-AAAA-TGTCCG	-CATAGG-GA-GAATGTCCG		A	D	
SEQ ID		213					215						145						217						9,11	1,3	5,7	
	1a	1P	$1^{\rm c}$	Ic	2a	2b	2 p	2 b	2°C	20	2α	7 0	2d	32	38	3a	3а	За	3а	За	3a	3a	За	3a	ಇ	3a	3a	
	HCV-1	BE90	2TY4	4TY4	HC-J6	HC-J8	NE91	EB12	ARG6			T983		E CHR20		CHR22		LI 26	NE93	NZL13	EB1	EB2	EB3	EB7	BR33	BR34	BR36	

Н	4/111
8031 -CTGAG-GTGAAGGCG-TA CCA-GGA-G-GTR-GAGTGA-CTAG	
SEQ ID	108 110 1110 1116 2001 2003 2003 2003 2010 1159 1159
3b	4 4 4 4 4 4 4 4 4 4 4 4 4 5 5 5 5 5 5 6 6 7 6 7 7 7 7 8 8 8 8 8 8 8
T10 BE98	GB46 GB116 GB115 GB328 GB328 GB328 GB328 GB328 GB328 GB328 GB2438 GB BB32 GB BB35 GB26 CHR19 GB116 GB113 GB26 CHR19

gure 1 - Continued 4

8032	AGGCTTTATGTTGGGGGCCCTCTTACCAATTCAAGGGGGGAGAACTGCGG	C	AT-GCCA-	AT-GCTGCT-GTAAC	ACGAGCA-GTTCAGC-ACCC	ACAAGCA-GACAGC-AA	ACCGAGCA-G-TA	ACCAAGCA-GA	-CAG-	-CAGCA-GACAGC-A	-CA	AACGAGCA-GACAGC-AACTC	CGAGCA-GCTACAGC-AAC-A-C	CCTGCA-GTTCAGC-ACCC-GT	-AGC-A	-CAGC-A	-CAGC-A	CCTGCAA-GTACAGC-ATCC-GT	-AA-GTTTCAGC-A	CCTGCA-GTTCAGC-ACCC-GT	CCTGCCA-GTTCAGC-ACCC-GT	CCTGCCA-GTTCAGC-AACCC-GT	1	CAGC-A	CCTGCA-GTTCAGC-ACCC-GT	CCTGCA-GTTCAGC-ACCC-GT	CCTGCA-GTTTCAGC-AACCC-GT	CGCA-CATCA-GTACAGT-ACTCC-G
	1a	15	10	10	2a	2b	2b	2b	20	2 2 2	2 _C	20	2d	3a	3a	3a	38	3a	3a	3a	3a	3a	3a	3a	3а	За	3a	35
	HCV-1	BE 90	2TY4	4TY4	HC-J6	HC-J8	NE91	co EB12	S ARG6	IIS ARG8	110 110	T983	H NE92	CHR20	2 CHR21	F CHR22	딘 26)	_T7	NE93	NZL13	EB1	EB2	EB3	EB7	BR33	BR34	, BR36	T9

CGCA-CATCA-GTACAGT-ACTCC-G CCTGTTA-GTTCAGC-AAC-AC	ACCGCTCA-GCATCAGC-AACCTGACGGC-TCA-GCATCAGC-AACCTGACGC-TCA-GCATCAGC-AACCTGACGC-TCA-GCATCAGC-AACCTGACGC-TCA-GCATCAGC-AACCTTTACGC-TCA-GCATCAGC-AACCTTTACGC-TCA-GCATCAGC-AACCTTTACGC-TCA-GCATCAGC-AACCTAACGC-TCA-GTACAGC-AACCTAACGC-GCCCA-GCAACCTAACGCCCCA-GCAACCTAACGCCCCCCACCTAACGCCCCCCCCCCC-
3c	4 4 4 4 4 4 4 4 4 4 4 4 4 5 5 5 5 5 5 6 6 6 6
T10 BE98	GB48 GB116 GB115 GB315 GB809 GB809 GB809 GB809 GB809 GB804 GB843 GB643 GB70 GB GB43 GB GB-13 GB GB G

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8131 8131	1b TCATGGGGCC	1bC-AAGGT-	10CTC	10TTCCCC	2a GCA-GC-T	CA-GC-TATT-CCC	TCA-GC-TATTT-CCC	CATII-CIC	GCA-GC-TAGCC	GCA-GC-T	GCA-GC-TA-	TCA-GC-TTGG-	B-	TC-TTTTA	C-TA-	TTATC-TC	TCTCTACC-TC	C-C-CTCTACC-	TC-LT	TC-TTCTATC-TC	T	-TATC-TC	3a TTC-TT	TC-TTCTATC-TC	3a TC-TTTCTATC-TCT-TCC	3a TC-CTCTATC-TCTCC	3a TC-TTC-TATC-TCTCC	3bC-CCCTCTC-TCTCC-T-	
,	1p	15	10	10	2a	2b	2b	2b	2c	2c	2c	2c	2d	За	3а	3a	3a	3a	3a	39	3а	3a	3а	3a	3a	3а	3a	3Ъ	
1 1011	HCV-J	BE90	2TY4	4TY4	HC-J6	HC-J8	NE91	EB12		ARG8			_		7 CHR21	E CHR22	E E	<u>ائ</u> 26)	NE93	NZL13	EB1	EB2	EB3	EB7	BR33	BR34	BR36	T9	

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8131	
8082 C-C-C	G
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T10 BE98	GB 48 GB 116 GB 116 GB 116 GB 215 GB 215 GB 219 GB 219 GB 219 GB 219 GB 219 GB 219 GB 2119 GB

8132 8181	CCCTCACTTGCTACATCAAGGCCCGGGCAGCCTGTCGAGCCGCAGGGCT	oTT-GT-G	TATC-AT	3 -TC	-TCTA	AATG-G-	oA-GATATTGAAGTA	oA-GGTATTGAAA		-AGG-G	-AG		-ATGT	1AGG-GA-AAAAGTGCA-A	-AAT	-AATTTA-AGTGCGAAG	AATATA-AGTGCCGA	-AATTACAGTGCGAAG		AATCACAA-GGCGAAG	-AAT	•	-AAT	•	-AAT	- AATTACAGTGCAAAC	-AAACAGTGCAA-GC	- AATAACAGGCAAA	-AA-ACTACTA-CA-GTGT
	1a	1p	1p	1c	10	2a	2p	2b	Sp	2 7	2G	2 2 2	2c	2d	32	3a	3a	3 9	32	3a	32	3a	3a	38	39	3a	3a	3a	3p
	HCV-1	HCV-J	BE90	2TY4	4TY4	HC-J6	HC-J8	NE91	EB12	S ARG6	SE ARG8	110	T983	S NE92	五 CHR20	CHR21	CHR22	E 2	LI 26)	NE93	NZL13	EB1	EB2	EB3	EB7	BR33	BR34	BR36	T9

8132 -AA-A-C-TACT-GA-CA-G-T-G-T -AAC-TA-AAATACCAAT-C-AA-T	TCAC TCAC TCAC	-AA-GGC-TTCAATCA-GTGA -A-CGGC-TATCAATCA-GTGG -TGGTT	-GG	$\begin{array}{cccccccccccccccccccccccccccccccccccc$
3b 3c	4 4 4 4 . 0 0 0 0	4 4 4 4 4 0 0 11 12 12 13	4 4 4 4 1 4 5 X X	വ മ മ മ മ മ മ
T10 BE98	GB48 GB116 GB215 GB358	GB809 GB809 G22 GB549 GB438	CAR4/1205 THE CAR1/501 THE EG-13	(92 BE95 BE96 CHR18 CHR19

Figure 1 - Continued 10

8231	CAGGACTGCACCATGCTCGTGTGTGCCGACGACTTAGTCGTTATCTGTGA	AACAC-T	CGC-T			GACTGTCCA	AC-GC	-GAC-GCCG						-GCTCTCCA	'TCCATTC-GGG-GGC	CCATTC-GTGG-GGC	-TCCATTC-GTGG-GGC	-TCCATTC-GAG-GGC	TC-G	CATT	.TCCATTGGG-GGC					-CATTG		TCCATTC-GGG-GGC	TCCATGGG-A-C	
8182	CAGGACTGCACCATGCT		g	-G		ATT-CGCCA	Ħ	ł	GTCC-GTT	GTT-C-CC	GTT-CTCC	GTI-CICC	GTT-CT-C	ATT-C-CCG	-G-ACCGGA-T-T	-G-AC-CCGGA-T-T	-G-ACCGGA-T-T	-G-ACCGGA-T-T	-G-ACCGGA-T-T	-G-ACCGGA-T-T	-G-ACCGGA-T-TTC	-G-A-TCCGGA-	-G-ACCGGA-	-G-ACCGGA-	-G-ACCGGA-	-G-ACCGGA-T-T5	-G-ACCGGA-T-TTC-	-G-AG-CCGGA-T-T1	A-ACCAT-TT-CTCA-	
	1a	1 p	1p	10	10	2a	2b	2b	2b	2c	2 0	2 c	2c	2d	3a	3a	3a	3a	3a	3a	3a	3a	3a	. За	За	3а	За	За	3b	
	HCV-1	HCV-J	BE90	2TY4	4TY4	HC-J6	HC-J8	NE91	EB12					NE92				-			NZL13	EB1	EB2	EB3	EB7	BR33	BR34	BR36	6L	
										٠,				- 0			1110	~	40)											

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8182 A-ACCAT-T-C-T-C-C-AT-G-G-G-G-G-C- A-AA-TCCAT-AT-C-T-C-G-A-TGG-TGC	AGA
3b A-7 3c A-7	Ф Ф Ф Ф Ф Ф Ф Ф Ф Ф Ф Ф Ф Ф Ф Ф Ф Ф Ф
T10 3 BE98 3	GB48 GB116 GB215 GB358 GB809 GAM600 G22 GAR59 GB549 GB549 GG13 GG13 GG13 GG13 GG13 GG13 GG13 GG1
	SUBSTITUTE SHEET (RULE 26)

8232 8271	AAGCGCGGGGTCCAGGAGGACGCGGGGAGCCTGAGAGCC	GTAACTGCAC	AACAT-	GCAAC-GA-CGA	GCAATAA-GA-CGA-AT	GCATAA-GA-CGA-AT	GTCAAC-GA-CGAAC	GI-AICG-CIAGAAGC	GT-ATCG-CTAGAA-AGCC	GT-ATCA-TTAGAAGCG	GATCG-TTAGAAGC	GT-ATCG-CTAG-AGC	GT-ATCG-CTAGAAGC	GT-ATCG-TTAGAAGC	GT	GT	GT	IGCCAGAAGCTC	TGCCAGAAGCTC	GTAAG-TAGA
	1a	1 p	1p	2a	2p	2b	2d	3a	За	3a	38	38	3a	3a	38	3a	32	3b	3b	30
	HCV-1	HCV-J	BE90	HC-J6	HC-J8	NE91	NE92	S CHR20		CHR22	TI UI	7⊥ E \$	HI NE93) NZL13	INBR33	H BR34	(9) BR36	T9	T10	BE98

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8232 8271	GATCAGAAACGACCCG	ATCAGAAACGAGCCG	GATCAGAAACGAGCCGT-	GATCTGAAACGAGCCG	GGICIGAA-CGAGCCGI	GICGAA-CGAGCCGI	ATTG-ACGCCGAGCCGT	GGCCAGTAAGAGCCC	GICGGCCGAGCCC	GATTCA-AG-CAA-CAAGCCC-NA-T	GCTGGTC-CANA-CNNCC-N	GCAACACT-AAA	GCAACACT-AAA	GCAACGCTAAA	GCAAACGCT-AATT-
	4°C	4Ω	4℃	4 C	4e	4e	4£	49	4 h	4 j	4.	Sa	5a	5a	5a
	GB48	GB116	GB215	GB358	GB809	CAM600	G22	GB549	GB438	CAR4/1205	CAR1/501	BE95	BE96	CHR18	CHR19
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SUBSTITUTE SHEET (RULE 26)

	RLYVGGPLT	N	X	K-D-ANK	RSRA-S-PEE-HTH	RK-OSR-S-PQBTV-H		-				RSLA-S-PBTH	QVEN-E-EKV-SCMFK-AO		QVEN-E-BKV-SCMFK-AQ	÷	1	1	NQVEN-E-EKV-SCMFK-AQ	N-E-EKV-SCMFK-AQ	1	K-B-BKV-SCMFK-AQ	K-B-BKV-SCMFK-AO	K-MPK-AQ	K-WFK-AQ	K-WFK-AO	1	1	AKDERV-TCMFK-QH
000	OEC TE	214					216					146						218						10,12	2,4	8'9			150
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Figure 2	HCV-1	BE90	2TY4	4TY4	HC-J6	HC-J8	NE91	EB12	ARG8	110	T983	NE92	CHR20	CHR21	CHR22	TI	T7	NE93	NZL13	EB1	EB2	EB3	EB7	BR33	BR34	BR36	T9	T10	BE38

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2694				1		1	ł		WHDT	MYK-DL	- ;		MFK-DL		QCMYK-QQ	OFCMYK-00	0CMYK-00	
2645	VKTA	VS-ELEKV-TA	KVEVE-EKTA	KVEVB-ERTA	KVEVE-E-KV-TA	KVEVE-EKTA		RVEVB-EKV-TA	RVEVE-ET-KV-SA	R	RVEE-EKV-SA	PR-X-VEVN-EXDX-KV-NA	X-RGBVE-BKV-TAMFK-DL-		HMSQ-EAR	AHLSSQ-DAR	HMSSLY-Q-ERQCMYK-00	HMSSI-V-O-H
			107	109	111	113	117	202	204	115	208	210	212		160	162		
	4 a	4a	4°C	4 C	4°C	4°C	40	46	4£	49	4ħ	41	4.		Sа	5a	5a	ď
	EG13	EG19	GB48	GB116	GB215	GB358	GB809			GB549	GB438		CAR1/501		BE95		CHR18	
								S	UB	STI	TU	TE	SHE	ET	(R	UL	E 2	6)

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7	:																													
7695	YRRCRASGVLTTSCGNTLTCYIKARAACRAAGLQDCTMLVCGDDLVVICE	NKKN		R		VLKIIAP	KIV-PV	IK		NN	IVAP-	VMVKN-V-IVAS-	FMIVQKIIAPS-			PFIABRNPDFVA-	?ITAKRNPDF	FITARNPDF	I	PFITAKN-RNPDFVA-					ł	PFITARNPDFVA-				A-
	1a	1p	1 p	10	10	2a	2b	2b	2p	2c	2c	2 _C	2d	3a	3a	3a	3a	3a	3a	3a	3a	3a	3a	3a	3a	39	3a	3b	3b	30
	HCV-1	HCV-J	BE90	2TY4	4TY4	HC-J6	HC-J8			S ARG8								LI 26)	NE93	NZL13	EB1	EB2	EB3	EB7	BR33	BR34	BR36	T9	T10	BE98

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CB48		2444 A	B	A-	-W	B	-			B-	1	; cs	•			A	H-A		VTA	
GB48 GB116 GB215 GB215 GB215 GB58 GB58 GCAM600 GCAM600 GCAM600 GCAM602 GCAM600		LSIKR	ISIR	LSISR	LSIR	ESIK	LSIK	FLTTKK	KG-S	LTTK	LTT	LTTK	LTIR	ITK-S-		L-SR-RL	R-Y-L-	I-SI	SI	
GB48 GB116 GB215 GB215 GB58 GB58 GB609 CAM602 CAM602 CAM622 GB549 GB438 GGR1426 CAR1/501 GGR19	2695	-	1	- 1				X	QYV	LVV	IYF	OEE	FF							
0.10		4°C	4c	4°	4°C	4e	4e	4£	49	44	41	47	47	4k		Sa	5a	5a	5a	
		GB48	GB116	GB215	GB358	GB809	CAM600	CAMG22	GB549						SH	H BE95) BE36	CHR18		6

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CCV-1 CCV-7 EB90 LD 11b CC-VG CC-VG EB91 EB92 CC-VG EB92 EB92 CC-VG EB93 EB93	Figure 2	- Continued	1ued 4
7 2 2 2 2 2 2 2 2 2 2 2 2 2 2 2 2 2 2 2	HCV-1	1a	SAGVOEDAASLRA
2 2 2 2 2 2 2 2 2 2 2 2 2 2 2 2 2 2 2	HCV-J	1b	T
2 2 2 2 2 2 2 2 2 2 2 2 2 2 2 2 2 2 2	BE90	1p	ΛT
2 2 2 2 2 2 2 2 2 2 2 2 2 2 2 2 2 2 2	HC-J6	2a	-Q-TEERN
20 20 20 20 20 20 20 20 20 20 20 20 20 2	HC-JB	2p	å
	NE91	2b	O-NB
11 3a 3a 3a 4 5 5 5 5 5 5 5 5 5 5 5 5 5 5 5 5 5 5	NESZ	20	\circ
2 3 3 3 3 3 3 3 3 3 3 3 3 3 3 3 3 3 3 3	CHR20	38	-DBR-A
2 3 3 3 3 3 4 5 6 6 6 6 6 6 6 6 6 6 6 6 6 6 6 6 6 6	CHR21	Зд	DD
3 3 3 3 3 3 3 3 3 3 3 3 3 3 3 3 3 3 3	CHR22	За	-DNR-A-G-
3 3 3 3 3 3 3 3 3 3 3 3 3 3 3 3 3 3 3	TI	34	DD
3 3 3 4 - D- 3 3 8 8 - C- 3 3 8 7 - C- 3 5 7 - C- 5 7 - C	T7	3a	-DDRTA
3 3a - D- 3 3a - 3 3 3b - C- 3 3b - C-	NE93	3a	-DDR-A
338	NZL13	3a	-DDR-A
38 38 38 38 38 38 38 38 38 38 38 38 38 3	BR33	3a	1
3a 3b 3b - C	BR34	3a	ı
3b - C-	BR36	3а	ı
3b -C-	419	3р	E-
75 865	TIO	3p	-E-E-
200	BE98	30	IDR-

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	- Continued 5	2745 275 4C -DBKRP-G- 4C -DBKRA-G- 4C -DBKRA-G- 4C -DBKRA-G- 4E -GBKRA-G- 4E -GBKRA-G- 4F -GBKRA-G- 4F -GBKRA-G- 4A -GBKRA-G- 4B -GBKRA-G- 4B -GBKRA-G- 4B -GBKRA-G- 4B -GBKRA-G- 4B -GBKRA-G- 4C -GBKRA-G- AG -GBKRA-GB-	5a -Q-THE 5a -Q-THE-N	74 TIM C
77 55555555555555555555555555555555555	Figure 2 -	6 5 8 9 00 00 /120 /501	BE95 BE96	0 1 0000

SUBSTITUTE SHEET (RULE 26)

	0000 0000 0000 0000 0000 0000 0000 00	ATGAGCACGATCCTAAACCTCAAAAAAAAAAGGTAACACGAACG	DB	AA	AA	ATT	A-AT	ACTT		ACTAGCA-AS					C	A-A	51	TCGCCCACAGGACGTCAAGTTCCCGGGTGGCGGTCAGATCGTTGGTGGAG	CTTCT		CCCCC			AA	ATCA	CGTAC	CCATTTCTC	CCATTT	CTATCTCT	CTATC	CCATT	
OT CT	OEQ ID					143				147	191	163	165	193		151																
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0 20 57 7		HCV-1	HCV-J	HC-J6	HC-JB	NE92	EB1	NZL1	HCV-TR	BE38	GB358	GB809	CAM600	GB724	EG-29	BE95		HCV-1	HCV-J	HC-J6	HC-J8	NE92	EB1	NZL1	HCV-TR	BE98	GB358	GB809	CAM600	GB724	EG-29	BE95

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Figure 3	- Continued	1 101
HCV-1	18	TTTACTTGTTGCCGCGCGCGCCCTAGATTGGGTGTGCGCGCGAGAA
HCV-J	1b	9L
HC-J6	2a	-A
HC-J8	2b	
NE92	2d	-A
EB1	3а	-AGACTC-T
NZL1	3a	-AGCAC
HCV-TR	3b	-ATGCTACACAGTAC-T
BE98	30	GC-AACCAGTAGT-C-C
GB358	4°C	9L
GB809	4 e	9-2L
CAM600	4e	9-JL
GB724	4.5	9-JL
EG-29	4.2	9-JL
BE95	5a	D-JL
		- L-
HCV-1	13	AAGACTTTCCGAGCGGTCGCAACCTTCAAGGTAAGACGTCAACGTCTAAGACTTTCAAGGTAAAAAGTTAAAAAGTTAAAAAGATTAAAAAAGTTAAAAAA
HCV-J	1p	
HC-J6	2a	GG
HC-J8	2b	TACGGTACCC
NE92	2d	AC
EB1	3a	ATAAGCACA
NZL1	3a	ATAAGCACA
HCV-TR	3b	
BE98	30	
GB358	4c	
GB809	4e	
CAM600	4e	
	4.7	GTCGA
EG-29	4.2	
BE95	Sa	GA

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110 201 4 60 20 4 60 60 60 60 60 60 60 60 60 60 60 60 60	AGCTACTGAA-AAAC	CACTA-TGAA-AA-A-A			GATATGAA'AA	251 CCCTCTATGGCAATGAGGGTGGGGTGGGCAGGAATGGCTCCTGTCTCCC	
Lontin 1a	2 7 ° ° ° ° ° ° ° ° ° ° ° ° ° ° ° ° ° °	3 2 G	33 33 33	4 4 4 4 D 0 0 6	54 C	2 2 2 2 2 2 2 2 2 2 2 2 2 2 2 2 2 2 2	0 4 4 4 4 8 8 8 8 8 8 8 8 8 8 8 8 8 8 8
HCV-1	HC-J6	NE92 EB1	NZL1 HCV-TR BE98	GB358 GB809 CAM600 GB724	EG-29 BE95	HCV-1 HCV-J HC-J6 HC-J8 NE92 EB1 NZL1 HCY-TE	BE98 GB358 GB809 CAM600 GB724 BG-29 BE95

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301	CGTGGCTCTCGGCCTAGCTGGGGCCCCCACAGACCCCCCGGCGTAGGTCGCG		ATCTCTCTATAA	CGA	AGACGTCAATACAC-	CCTATCTA-ATA-AC	CGCCC	TA-A-ATA-ACA-AC	C	CGGTCTT-ATT	CNN-GTCTATTN-GAC	CATCTA-ATTGA-A	AA-AA		351	CAATTIGGGIAAGGICATCGATACCCITACGIGCGGCITCGCCGACCICA		CGT		C			CTAATA	CCAAA	C		TTT
	la				2d						4e	42	Sa							2d					4e	43	5а
	HCV-1	HCV-J	HC-J6	HC-J8	NE92	EB1	NZL1	HCV-TR	BE38	GB809	S CAMEOO	C GB724	H BE95	SHE	EET	4) HCV-1	THEA-U	9L-DH 2	6) HC-78	NE92	EB1	NZL1	HCV-TR	GB809	CAM600	GB724	BE95

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Figure 3 - Continued 4	- Contin	ned 4
		401
HCV-1	1a	TGGGGTACATACCGCTCGTCGCCCCCCTCTTGGAGGCGCTGCCAGGGCC
HCV-J	119	TTT
HC-J6	2a	
HC-J8	3b	
NE92	2d	
NZL1	3a	
HCV-TR	3b	TAA
. GB809	4e	ACTACG-GTTCA
CAM600	4e	ACTACG-GTTC
GB724	4.2	AC
BE95	S B	TCAGGTCAT
		451
HCV-1	12	CTGGCGCATGGCGTCCGGGTTCTGGAAGACGGCGTGAACTATGCAACAG
HCV-J	1p	AT
HC-J6	2a	C
HC-J8	2 p	ACTTACGGA-ATC
NE92	29	CGA-AGA-A
NZL1	3a	CGACCTGA-AT-TC
HCV-TR	35	CTTGACAT-GGA
GB809	4e	AC-TTAC-GGA-CC
CAM600	4e	ATTAC-GGA-CT
GB724	4.2	N-G
BE95	5а	CACTGACTGGA

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	80		26	/111		
	ACGTGCGGCTTCGCCGACCTCATGGGGTACATACCGCTCGTCGGCGCGCCCC	-ATT	TT-T-T-T			-A
	SEQ ID NO		143	13,15,17 23,25,27 19,21		122,169 167 171 173 120,175 177
	2 2 2 2 2 2 2 2 2 2 2 2 2 2 2 2 2 2 2	13 15	28 25 25 26	3333 3333 3333 3333 3333 3333	4 4 4 4 6 0 0 0	4 4 4 4 4 4 4 4 4 4 4 4 4 4 4 4 4 4 4
Figure 4	HCV-1 HCVBC1 HCVHCT18 HCVHCT23 HCVHCT23	HCVTH HCV-J	HC-J6 HC-J8 NE92	TE SHEET (RULO NZILIS HCV-TR	GB809_4 GB116 GB215 GB358	GB809_2 CAM600 CAMG22 CAMG27 GB549 GB438 CAR4/1205

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α	143	6
4.2	Sа	S B
CAR4/901	BE95	BE100

Figure 4 : Continued 2

478 G		28	8/111	
429 TCTTGGAGGGCGCTGCCAGGGCCCTGGCGATGGCGTCCGGGTTCTGGAAG	CA-G	G-C-CTCA-TCG-A-A-CG-G-G-G-G-G-G-TCG-TG-A-CT-TG-A-GG-G-G-G-G-TT-TG-TCG-A-GG-G-G-G-G-G-G-G-G-G-G-G-G-	GG-A	AG-A
			Ç	CG-
n H H	1 1 1 1 2 2 1 1 2 2 1 1 2 2 1 1 2 2 1 2 2 1 2 2 1 2 2 1 2 2 1 2	2a 2b 2d	8 8 8 8 8 8 9 9 9 9 9 9 9 9 9 9 9 9 9 9	41.1 41
HCV-1 HCVEC1	HCVHCT18 HCVHCT23 HCVHCT27 HCVTH	HC-J6 HC-J8 NE92	HD10 BR33 BR36 NZL15 HCV-TR GB809 GB116 GB215 GB316 GB360 CAMG22 CAMG22 GAMG27 GAMG27	GB438 CAR4/1205
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Figure 4 : Continued 4

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528	GCTCTTTCTCTATC			CT		C		CL	L	CT	LD	L	CLT	CI	CLI		-ICC			-	CL	C L	L	CI	CC
	GGGAACCTTCCTGGTT						TGC	T-AC	TT-AC	T-GC	TT-GC	TT-GC	TI-GC	CL-GC	L	-	1	1	I	T	D			1	1
479	ACGGCGTGAACTATGCAACAGGGAACCTTCCTGGTTGCTCTTTCTCTATC						CC	GT-T-T	GA-ATCTT-ACT	GA-A	GA-AT-TCTT-GCC	GA-ATC	GA-AT-TC	GA-AT-TC	A	GA-TG	TA-TT	A-CT	GA-CTG	GA-CC	GA-CT	GA-T	GA-A	GA-TT	GA-CTC
	Ta	Тa	Тa	Тa	1a	1a	1b	2a	2 p	2d	38	ე ე	3 9	3a	3p	4a	4c	4°C	4c	4e	4e	4£	4£	49	4 h
	HCV-1	HCVECI	HCVHCT18	HCVHCT23	HCVHCT27	HCVTH	HCV-J	HC-J6	HC-J8	NE92	HD10	BR33	BR36	NZL15	HCV-TR	GB809 4	GB116	GB215	GB358	GB809 2	CAM600	CAMG22	CAMG27	GB549	GB438
										SU	BSTIT	UTE	E SI	HFF	T (RI	ÚF.	261								

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----G--A-----C-------GA-C--T--------GA-T----C------L------Figure 4 - Continued 5 44: 5a 5a CAR4/1205 CAR4/901 BE95 BE100

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529 TTCCTTCTGGCCCTGCTCTTGCTTGACTGTGCCCGCTTCGGCCTACCA TTCCTTCTGGCCTGCTTCGGCCTACCA TTCCTTCTGGCCTTCGGCCTACCA TTCCTTCTGGCCTTCGGCCTACCA TTCCTTCTGCTTCTTGCTTGCTTGCTTCGGCCTACCA TTCCTTCTTGCTTCTTGCTTCTTCTTCTTCTTCTTCTTCT	T-G	TTTA-TCCATAAG-TAGTCTAGTTTTA-TCCATAAG-T-GTCTAGT-T-TTTA-T-CATAAG-CAGTCTAGT-T-TTTA-T-CATAAG-CAGTCTAGTTTTAAG-CAGTCTAG-
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HCV-1 HCVHCT18 HCVHCT27 HCVHCT27 HCVTH HCVTH	HC-J6 HC-J8 HC-J8 S83 NE92	HD10 BR33 NZL15 HCV-TR

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529	CATGC-C-CGAGA-	9-B		ATTGCTA-CA	-ACTATGCTA-CAT	CTATTGCTA-CGT-A-	-ATTA-	- 4 - Ht	; A : : :	6	CTGC				CTTATGCC-ACAGTTC-G	1	- 1	TATTTTGTCCTGCTAGTT-C ATATGC-CCGCTAGTT-C GTT-C
	4a	4 a	4 b	4°C	4Ω	4°	4°C	4 0	4q	4e	4e	4 £	4 £	49	4h	41	4.5	ក ក ក ក ក ក ក ក ក ក ក ក ក ក ក ក ក ក ក
	GB809 4	Z4	Z1	GB116	GB215	GB358	Z6	27	DK13	GB809 2	S CAM600	G22	G27	GB549	O	语 CAR4/1205	N CAR4/901	98 3H SEC 99 SA4

579 628	AGTGCGCAACTCCACGGGCTTTACCACGTCACCAATGATTGCCCTAACT		C		ATCATT-	CC	GGTGT-CA-ATGCCT-C		AAGATGTACCGGCATGGCCA-CTG	CA-GATT-GTTCTAGCTCTT-AA	GCAAGGAGGC-ACTCCATGCCGCT-C	GCAAGAGCA-CTCATGACAGA	GTGGA-GT-TCCTGT-C-TCCTT-CTA	GTGGTA-GT-TCCTGT-C-TCCTT-CTA	GTGGTA-GT-TCCTGT-C-TCCTT-CTA	GTGGTA-GT-TCCGT-C-TCCTT-CTA	GTACACGA-GT-TCATGTGC-TCCTTG
	1a	1a	1a	1a	1a	Тa	1p		2a	3p	2c	2d	3a	3a	38	32	3p
	HCV-1	HCVEC1	HCVHCT18	HCVHCT23	HCVHCT27	HCVTH	HCV-J		HC-J6	HC-J8	883 ITU	NE92	HD10	RB33	BR36	6 NZL15	HCV-TR
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e 4 - Continued 9

823	CTGT-	-LGL	A	CT-	G	G	GCC	G	G	CCCIG	CB		IC		GCC		-L9	B	A	A
579	CTACGTG-TTCA-CTA	CTACGTG-TTCA-CTA	CIACGTG-TTCG-CTT	CTATGTCG-CTTA	CIATTGTCG-C	CTATTGTCA-CTA	CTATTGTCG-CT	- !	1	CTATTG-TTCGTA	CTATTG-TTCATA	TTAT-AATCA-CC	TTAT-AATCA-CTATC	CTACGAT-TCAT	CTACGTG-ATCA-CT	CTATTG-TTACGGTT-TA	CTACGTGT-TCA-C	CTACATGT-TATTT-	CIACAIGI-IA-CII	CTACAGT-TGTT
	4 a	4 a	4p	4°C	4°C	4°	4°	4°	4 d	4e	4 e	4£	4 T	49	4 h	41	4.2	Sa	Sа	5а
	GB809 4	Z4 _	Z1	GB116	GB215	GB358	26	27	S DK13	GB809 2	CAM600		8 G27		(B438	\sim	CAR4/901	BE95	BE100	SA4

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629 CGAGTALTGTGTGTACGAGGGGGCCGATGCCATCCTGCACACTCCGGGGTGC C	T		-ATAGCATGACC	ATCACC-GGC-ACTCCAG-CTGGTCC	ACCCACC-GGCCTCA-TCAG-TCTCTTA	-TCT-GGCCTT-AA-GAAG-GTTT-A-A	GTCCC-GGCCTCAGGTG-TTGTCCT	GC	GTG-G-C-TC-ATC-TTTG-G-CCT	GC	GC	GC
1 H	n n n		115	2a	2p	2 _G	2q	3a	3a	3a	3a	3p
HCV-1 HCVEC1	HCVHCT18 HCVHCT23	HCVHCT27	HCV-J	HC-J6	15 HC-78	383 UTI	IE SH	HD10	3) BR33	F BR36	92 NZL15	HCV-TR

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		629
GB809 4.	4a	-CCG-ACTAA-T-A-C-CCATATTTG
Z4 =	4a	-CACTAT-A-CCAATTG
21	4 b	-CCAAGC-CCAATTGAT
GB116	4 c	CAT-A-T-CCAACTCT
GB215	4°	CA
GB358	4°	1
92	4°	CATC-AAC-CCAGT-ACTCA
Z7	4c	CAATC-AAC-CCAACTCA
DK13	4d	CACTAA-C-ATT-CCAT-ACTCA
	4e	CAA-C-A-ACAT-ACTCA
S CAM600	4e	-ACAA-C-AAACAT-ACTCA
	4£	-TCAC-TTA-T-CCATCTAA
E G27	4£	-TCAC-TTA-AGCCATTCTAA-
	49	-TAT-A-T-A-CCATATCTAAT
13 GB4 38	4 h	-CTAC-A-CCAACTACT
2 CAR4/1205	41	-TCATAC-AGA-CCATCTT
F CAR4/901	4.2	-CCATAC-ATC-CCAATTAA
26)		
BE95	5 a	-TTCCACTA-ATA-CCTGAG-ATT-
BE100	5 8	-TTCCACTA-ATCTGAG-ATC
SA4	5a	-TTCCATT-ATA-CCTGTTG-AT

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679	GICCCTIGCGITCGIGAGGCCAACGCCTCGAGGIGITGGGIGGCGAIGAC						GCCGA-TTTTCC-TCAC-C-	GAGAAA-TGTA-ATCCA-ACG-CT-	AT-AGAATAATGG-AT-CATCA-ACAAG-A	T-AGACC-CTTC-ACG-TG-	T-AGGAGAATACC-CA-ACG-TT-	ATAGCTTA-ATGCCACCC-AG	ATC-AGCTA-GT-CACACCC-AG-A	A-ATC-AGCTA-AC-CCACCC-AG	ATC-AGCTA-AT-CCACCC-AG	GGACAACCCAACAA-AAACA
	٦a	Ja	ц	Тя	1a	1a	1p	2a	2 p	2 2 3	2d	32	3a	3a	3a	3b
	HCV-1	HCVEC1	HCVHCT18	HCVHCT23	HCVHCT27	HCVTH	HCV-J	HC-J6	HC-J8	S83	NE92	HD10	BR33	BR36		HCV-TR
								S	UB	STI	TUTE	SHE	ET	(RU	LE 2	26)

679AC	T-A-C-T-GA-G-TT-G-TCAG-AC-CCC-T- T-A-CGA-G-TT-G-TCAG-AC-CC	-A-C-T-GAAGACC-GCAGC	GTCATGACATT-TGAGTACCCAAT- GTCA-GA-A-ATT-TGAGTCCCAAT GTCA-GC-A-ATT-T-AGT-ACCCAAC
44 44 44 44 44	1 4 4 4 4 4 0 0 0 0 0 0	4 4 4 4 4 4 4 4 4 4 4 4 4 4 4 4 4 4 4	5 8 8 8 8 8 8 8 8 8 8 8 8 8 8 8 8 8 8 8
GB809_4 Z4 Z1 GB116	GB215 GB358 GB358 Z6 Z7 DK13	GB809_2 GB20 G22 G27 GB549 GB549 CAR4/1205 CAR4/1205	.00 BE100 SA4

- Continued 14

Figure 4

729 CCCIACGGIGGCCACAGGGAIGGCAAACTCCCGGGACGCAGCTTCGAC		CGGA-CAGCAA-AG	AG-ATGTGCA-C-GCC-GGCGCT-ACA-GGCT-AGA AC-ACTGTG-AAC-CCGGTGCG-T-A-TCGTAGCGA C-ATC-CTATC-ACCTGGCGCT-T-A-T-A-GGCGG	GC-ATA-ATGTGCC-ACCTGGTGCG-TTA-C-A-GGCGGA AAGTT-C-T-GG-GCAAA-CG-TTC-A-ACA	AAAGTT-C-T-GGGGGAAA-CG-TTC-A-A-CA AAAGT-A-T-C-T-GG-GCAAA-CG-TTC-A-ACA AAGTT-C-T-GG-GCAA-TA-TG-TG-TC-A-A-CA AA-GGTTACCCTTGGCG-GA-A-CG-TC-A-A-CA-A-C
1a 1a	1 n n n	1a 1b	22 22 20 20 20	3a 2d	3333 3333 3433
HCV-1 HCVEC1	HCVHCT18 HCVHCT23 HCVHCT27	HCVTH HCV-J	HC-J6 HC-J8 SB3		BR33 BR36 NZL15 HCV-TR

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	CCT-T-AGCC-AGCTT-GG-GCAGT-AG-T-CCGA CTT-AGCC-ACT-GG-GCGGT-AG-T-CTGA
4 4 4 4 4 4 4 4 4 4 4 4 4 4 4 4 4 4 4	വ വ
GB809_4 Z1	BE100 SA4

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928 GTCACATCGATCTGCTTGTCGGAAGCGCCACCCTCTGTTCGGCCCTCTAC 620 620 620 620 620 620 620 62	CGTCAGGAT-TCGCCTT CAGCAC-ATGAT-TCGGCT-GT CA
1 1 1 1 1 1 1 1 1 1 1 1 1 1 1 1 1 1 1	2000 3000 3000 3000 3000 3000 3000 3000
HCV-1 HCVBC1 HCVHCT18 HCVHCT23 HCVHCT27 HCVTH HCVTH	- 90-0-1 H CALL (MULE 26)

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779	-G1G-GCAA-GA1GCGG-G-GT-TT -ATG-GCT-AA-GACGCGTT-GTT	-GTG-ACA-GGTGCGTTA-GCT	TG-GA-GATGCTTTG-GCCTT-	-AG-GCAA-GGCGCTTTG-GCCTT	TG-GA-GATGCTTGCGCCTT	-ATG-GCA-GGCGCTTG-ACT	-ATG-GCA-GACGCTTAG-GCCT	G-GA-GGCGTCC	-CTG-GCA-GATGCTG-G-CCC-	TG-GCA-GATGCTA-GC	G-GTA-GGC-CTTAT-GCAA	TG-GTA-GAC-CTAT-GCCA	-GG-GCT-AA-GGTGCGCG	AGTG-GCA-GG-GCGT-ACT	CGTG-GCAA-GGGCGGCACCTT-T	-GTG-GTA-GGTGCATCT	-AGC-G-TCTACA-CGAG-GTGCCGT-A	-AGC-G-TTACT-GGAG-GTGCCGT-A	-GGC-G-TCTACT-A-CGAG-GTGCCAA
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	GB809_4 Z4	Z1	GB116	GB215	GB358	26	LZ SU	SS DK13	☐ GB809 2	T CAM600	\$ G25	H G27	GB549	GB438	CAR4/1205	© CAR4/901	BE95	BE100	SA4

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829	GTGGGGGACCTATGCGGGTCTGTCTTTCTTGTCGGCCAACTGTTCACTT		TTT	TTT			TTCACTCTCG	- THGGGGPGA-CGA-C	ATG-GG-CGA-GAC-ATCGGGCM	-0-10-00-00-00-00-00-00-00-00-00-00-00-0	A-AAGTCG-GGA-GT-G-CTTCTG-CT-A-	TTA-GTG-CCCBB	TTA-GTG-C	TA-GTGCGy	TTA-GTGCGAGC/	CGCT-TGGGCAGC
	Ta Ta	1a	1a	Тa	1a	1a	1p	2a	Sp	2 2	2đ	3,8	3a	3а	3a	3p
	HCV-1	HCVEC1	HCVHCT18	HCVHCT23	HCVHCT27	HCVTH	HCV-J	HC-J6	HC-J8	883 ITS	ALL NE92	HD10	T BR33	28 BR36	II NZL15	(92 HCV-TR

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	C A	CGA-	CA	,9-I	CI-G	B-I	GT-G	I-G	CI-G	CI-G	GI-G	CA-C		GG	CT-G-C7	T-G-CC	CAC	Ę	75-L)
	TACTAGGCTCAGGGA	T	A-TATGTAGGCCAGGGA	A-CGTGGCAT-GTGATT-T-	A-TT-GT-TGGCACT-GTTGATT-T-	A-CAGTGGCAT-GTGAT-T-	TATGTGGCACT-GTGAT	A-T	A-CAG-GTGGGCT-GT	CCGTGGCT-ACT-GAA	A-CCT-GIGGCT-ACT-GGA	T	A-TATGAGGCA-AA-GGAA	A-CATAGGCGGGA	A-CAATAGGCT-G-CAGGAGGT	A-TATGGGGT-G-CGTA	CAGACTAGGCAGA	7	AAG-GIG-BC-BCI-GA	:
	AC	C	ATG	9	B-L	AG	ATG	B	AG-G	CG	CI-G	B	ATG	AP	AAT	ATG	AC7	7	5000 4	
829	I	I	A-T	A-C	A-T	A-C	I	A-T	A-C	C	A-C	I	A-T	A-C	A-C	A-T	C	6	7 E	
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	GB809 4	l		16	15	58		-	3	09 2	600			49	38	CAR4/1205	CAR4/901	ı	00	
	GB8	24	21	GB116	GB215	GB358	92	Z Z Z	SORI	∃ GB809 2	E CAM	£ G22	# G27	GB5	GB4	CAR.	CAR	Ē	BE100	

879 CTCTCCCAGGCGCCACTGGACGACGCAAGTTGCAATTGCTCTATCTA		ATC-C-GT-TGAGTAAA	GACAATTTGTAC	GGACAA-ATAC-TTTGTCG-AACTCAC- GCAATTAA-TTTGTCG-ACCTCAC-	-AGATC-TTCAAGTCGACCTCAC-GC- -AGAC-CTCAAGTCGACCTCGC-GC-	-AGATC-TTCAAGTCGACCTCGC-GC-	-AGATC-ATCAAGTCGACCTCGC-GC-	-AGATC-CACCGTGACGCGAC-
H H	1 H H	1a 1b	2a 2b	2c 2d	8 8 8 8	39	დ	39
HCV-1 HCVEC1	HCVHCT18 HCVHCT23 HCVHCT27	HCVTH HCV-J	111188 111188 111188	S83 NE92	HD10 BR33	9E BR36	NZL15	HCV-TR

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	1 1 1 1	-D	CGAGC-CGC-	CAGGC-A	1		-CAGGC-AT-	1	1		-CAAGC-ATC-TG-ACTC-CA	-CGGC-C-TTG-AG	-AGGC-C-TGC-C-G-AG	-CGGGC-CTTC-G-ACC	CAACTTCG-A	-CGGAC-CATTTGAACTG-AC	-CAGGC-C		TAGGTC-C-AGGCTGTGAACCTCA	TAGGTC-C-AGTGCTGTG-ACCTCCA	ウー・・・・・・・・・・・・・・・・・・・・・・・・・・・・・・・・・・・・・
879	-CAGG	TCGGG	-CGAG	-CAGG	- CGG B	-CAGG	-CAGG	-CAGG	-CAATC-C	-CAAG	-CAAG	DDD-	AGG	5550-	-CAA	- CGG A	-CAGG		TAGGT	TAGGT	
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	GB809 4	Z4	21	GB116	GB215	GB358	92	5 Z7		GB809 2	CAM600		E G27		≅ GB438	_	2 CAR4/901		BE95	BETOO	+170

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929 CCGGCCATATAACGGGTCACCGCATGGCA CCGGCCATATAACGGGTCACGCATGGCA	-T - TACC - C - T - A G AA - T - C - C - C - C - T A -A C - T - A T -A C - TT - A - T - A T -A C - TT - A - T - A T -A C - TT - A - T - A T -A C - TT - A - A - T - A T -A C - TT - A - A - T - A T -A C - TT - A - A - T - A T -A C - TT - A - A - T - A T -A C - TT - A - A - T A T
1 1 1 1 2 2 2 2 2 2 2 2 2 2 2 2 2 2 2 2	200 200 200 300 300 300 300 300 300 300
HCV-1 HCVHCT18 HCVHCT23 HCVHCT27 HCVTH	HC-J6 HC-J8 S 83 S 83 S 83 HD 10 B 83 HD 10 WZILE HCV-TR

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23	957	G-TCCDG
- Continued	99 9 9 9 9 9 9 9 9 9 9 9 9 9 9 9 9 9 9	5a GT- 5a GT- 5a GT-
Figure 4 -	GB809_4 Z4 Z1 Z1 GB116 GB215 GB358 Z6 Z7 Z7 DK13 DK13 CAM600 G22 GAM600 G22 GAM600 G27 GB438 CAR4/1205 CAR4/1205	BE95 BE100 SA4

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D 1 MSTNPKPAKKNKRNTNRRPADVKFPGGGQIVGGVYLLPRRGPRLGVRATR	R-1	R-T1	R T N N N N N N N N N
SEQ ID	144	148	192 164 166 194 152
1 2	2a 2b 2d	3a 3b 3c	4c 4e 4? 5a
HCV1 HCVJ	HCJ6 HCJ8 NE92	EB1 NZL1 HCV-TR BE98	GB358 GB809 CAM600 GB724 EG-29 BE95

Figure 5 - Continued 1

	KTSERSAPRGRRAPIPKAR RPEGRTWAA PGYPWPLYGNEGGGWAGWLLSP		¥	S. S	
V-core	RPEGRTWAQ	-ST-KS-GK -ST-KS-GK T-KS-GK	. S		Q-TS-G-
51	KTSERSQPRGRRQPIPKAR		-SS -SS -SS -SS		
	1a 15	23 24 24 24	3333 3593	75 75 76 76 76 76 75	5a
	HCV1 HCVJ	HCJ6 HCJ8 NE92	EB1 NZL1 HCV-TR BE98	GB358 GB809 CAM600 GB724 EG-29	BE95

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101 126 1a RGSRPSWGPTDPRRRSRNLGKVIDTL 1b	3a	4e	5a
1a 2b 2d 2d	35 30	4e 4e 4?	5a
HCV1 HCVJ HCJ6 HCJ8 NE92	NZL1 HCV-TR BE98	GB809 CAM600 GB724	BE95

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127 TCGFADLMGYIPLVGAPLGGAARALAHGVRVLEDGVNYATGNLPGCSFSI	- X-	\(\lambda \). \(
<u>~ ~ ~</u>	<u> </u>	288	3a 2d 3a	3a 3b
HCV-1	HCVHCT18 HCVHCT23 HCVHCT27 HCVTH	HCV-J HC-J8	NE92 HD10 BR33	BR36 NZL1 HCV-TR

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nued 4	127		II		III	III	III	IYN		I	II		AIAVIAVI	
Contir		4а	4c	4c	4c	4 е	4е	4 £	4£	6 4	4h	41	4 5	5a 5a
Figure 5 · Continued 4		GB809 4	GB116	GB215	GB358	GB809 2	CAM600	CAMG22	CAMG27	GB549	GB438	CAR4/1205	CAR4/901	BE95 BE100

Figure 5 · Continued 5

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226			
0	PGC	1111	11111
V2	CPNSSI VYEAADAILHT	TWQLQA-VV TWQLTVL -WQLEG-V	D-VA
·	TNDCPNSSI	T	S S S S S
E1 V1	YQVRNSTGLYHVS H	AE-K-1STG-M- VE1SSS-YAS-N TWQLTVL VE-KDTGDS-MPS	LEW-TSVL LEW-TSVL LEW-TSVL LEW-TSVL LEW-TSVL
177	FLLALLSCLTVPASA YQVRNSTQLYHV TNDCPNSSI (VYEAADAILHT PGC		FIHAS LEW-TSVLSD-VFIHAS LEWTSVLSD-VFIHAS LEWTSVLSD-VFIHAS LEWTSVLSD-VFIHAS LEWTSVLSD-VFIHAS LEWTSVLSD-V
	<u> </u>	2a 2b 2c 2d	3a 3a 3a 3b
	HCV-1 HCVEC1 HCVHCT18 HCVHCT23 HCVHCT27 HCVTH	HC-J6 HC-J8 S83 NE92	HD10 BR33 BR36 NZL1 HCV-TR

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Figure 5 · Continued 6

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226		7
٧2		-LDAML
	V - A - A - A - A - A - A - A - A - A -	
7	EHY AS-1 1 EHY AS-1 1 VHY AS-1 1 VHY AS-V 1	LTYGSL
177	9 - 1 - 1 - 1 - 1 - 1 - 1 - 1 - 1 - 1 -	
*	4 4 4 4 4 4 4 4 4 4 4 4 4 4 4 4 4 4 4	6 a
	GB809_4 24 21 21 21 21 21 21 22 22 25 27 27 27 27 27 27 27 27 27 27 27 27 27	HK2

Figure 5 · Continued 7

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276 PUTATIVE	LLVGSATLCSALY	MV-M MI-MAA II-MV	MA-M
	LRRHID		1 - S - V - V - V - V - V - V - V - V - V
74	TRDGKLPATQ	VQQPGALTQG VKHRGALTRS ISQPGALTKG VSQPGALTKG	V-YVGATTAS V-YVGATTAS VKYVGATTAS V-YVGATTAS
	TPTVA	S-N N A-NL- S-NI-	s
V3	VPC VREGNASRCAVAM TPTVA TRDGKLPATG LRRHID LLVGSATLCSALY	EKVTIPV S-N VQQPGALTQGT MV-M	ad - T - A - TPV
227	V P		
	<u> </u>	25 25 24 25	3a 3a 3b
	HCV-1 HCVEC1 HCVHCT18 HCVHCT23 HCVTH HCVTH	HC-J6 HC-J8 S83 NE92	HD10 BR33 BR36 NZL1 HCV-TR

SUBSTITUTE SHEET (RULE 26)

Figure 5 - Continued 8

276 PUTATIVE	F V - M - A - V - V - V - V - V - V - V - V - V	AV- Y-A-G-A AV- YG-A AV- Y-A-G-A	
γ,	AVSMDA-LES VAHPGA-LES APYDNA-LES APYTGA-LES APY1GA-LES APY1GA-LES APY1GA-LES APY1GA-LES SPYGA-LEP SPYGA-LEP APY1GA-LES APY1GA-LEP APY1GA-LEP APY1GA-LEP APY1GA-LEP APY1GA-LEP APY1GA-LEP APY1GA-LEP APY1GA-LEP APY1GA-LES APY1GA-L-S	APSLGAVTAP APSFGAVTAP APNLGAVTAP	IDMAST G F
	18		- N-1
٨3	MT-11PV	-MTVQI KD-VQI QD-V-KQI	T-900V
227			-
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	GB809_4 24 21 21 21 21 6B16 6B215 6B215 7 7 7 DK13 6B809_2 CAM620 CAM620 CAM620 CAM627 GB549 GB549 GB549 GA738 CAR4/1205	BE95 BE100 SA4	271

Figure 5 - Continued 9

319	SPRRHWTTQG CNCSIYPGHITGHRMA	H	SA S1] S1]
۸۶	SPRRHWTTQG	QHFV-D QNFE QH-TFV-E QH-KFV-D	RQ-V-T RQ-V-T RQ-V-T RQ-V-T
277 TRANSMEMBRANE DOMAIN	VGDLCGSVFLVGQLFTF SPRRHWITQG CNCSIYPGHITGHRMA	G-M-AA-M-IVQHFV-DTVAIILS-A-MVQNFEQVALM-AA-VVVVQH-TFV-ER IA-M-AS-V-IIQH-KFV-D	
	<u>च्या व्याप्त</u> प्रमास	2a 2c 2d	3a 3a 3a 3b
	HCV-1 HCVEC1 HCVHCT18 HCVHCT23 HCVHCT27 HCVT4	HC-J6 HC-J8 S83 NE92	HD10 BR33 BR36 NZL1 HCV-TR

Figure 5 - Continued 10

319			1
٧5	0 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0	RQ-A-V-N RQ-A-V-D RQ-T-V-D	qV-D
	1 1 2 2 2 2 2 2 2 2 2 1 1 1 2 1 2 1 2 1		-:-
277 TRANSMEMBRANE DOMAIN		AALM- AALM-	ILA
	73 - 1 - 1 - 1 - 1 - 1 - 1 - 1 - 1 - 1 -	5a 5a	6 a
	GBB09_4 24 21 21 21 21 68116 6B215 6B358 2 2 2 2 2 2 2 2 2 2 2 2 2 2 2 2 2 2 2	BE95 BE100 SA4	HK2

4648	GTGTGCCAGGACCATCTTGAATTTTGGGAGGGCGTCTTTACAGGCCTCACI			ATAA	-ACTCACTAA	←	7997			4599	CATATAGATGCCCACTTTCTATCCCAGACAAAGCAGAGTGGGGAGAACCTT	C	CA	CTC	CCAGACTCTCAGACTCT-C	CAGACTCT-C	CAGACTCT-C	ACAGACTCT-C	ACAGACTCT-C	4731	
	HCV-1	HCV-J	HC-J6	HC-J8	HCC153	EB1	EB2	EB6	12 EB7	ibs:	III HCV-1	HCV-1	원 - 16	HC-18	到 HCC153	EB.	(92 (92	EB6	E87		

Figure 6

Figure 6 - continued 1

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HCV-1 HCV-J HC-J8 HCC[53 EB1 EB2 EB6	4751 CCTTACCTGGTAGCGTACCAAGCCACGTGTGCGCTAGGGGCTCAAGGCCC -C
HCV-1 HCV-J HC-J6 HC-J8 HCC53 EB1 EB1 EB2 EB6	4801 TCCCCATCGTGGGACCAGATGTGGAAGTGTTTGATTCGCCTCAAGCCCA A-T

Figure 6 - continued 2

4900	SECECTETTCAGAAT	ACA	TACCC	TCGACC	CC	-CA	-CA	-CA	-CA	-CA	←	4892				
4850	CCCTCCATGGGCCAACACCCCTGCTATACAGACTGGGCGCTGTTCAGAAT	-AG	-AGTGCCTCGC-CTTACCC	-AGACTCCCGC-CTTCGACC	-AAGCTTTC-GTGCCA	←	4863				-AACATGTC	-AAATGTC	-AT-AACGTC	-AT-AACGTC	-	4878
SEQ ID NO					53	31	33	35	37	39						
	HCV-1	HCV-J	HC-16	HC-18	HCC153	HD10-1-25		器 BR36-20-164		H BR36-20-165	# EB1	H EB2	E EB6	EB7	6)	

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continued 3	4949 GAAATCACCCTGACGCACCCAGTCACCAAATACATCATGACATGCATG	4950 GGCCGACCTGGAGGTCGTCACGAGCACCTGGGTGCTCGTTG
Figure 6 - continued 3	HCV-1 HCV-J HC-J6 HC-J8 HC-L3 HCC153 HD10-1-25 HB136-20-164 BR36-20-166	(35 a) HCV-1 (36 a) HCV-1 (46 - J6 (46
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4991 5040	GCGGCGTCCTGGCTGCTTTGGCCGCGTATTGCCTGTCAACAGGCTGCGTG	AA	-GGTGCG-CCG-GCGTT	-GGGACCGATCG-G-GTA-T	-AGCGCC-AGCCTGTCT	-AGCGCC-AGCCTGTCT	-AGCGCC-AGCCTGTCTT	-AGCGCC-AGCCTGTCTT	-AGCGCC-AGCCTGTCTT		5041 5090	GTCATAGTGGGCAGGGTCGTCTTGTCCGGGAAGCCGGCAATCATACCTGA	T1-1-1-1-1-1-1-1-1-1-1-1-1-1-1-1	TGCA-CC-CT-GCA-G-TAA-CA-CGAG-C-TCG-TGCG	TCCA-TC-CC-ACA-CAAT-ATCG-GTTTG-GGCCC	ACTCATAAGCGGGCCG-TA	ACTCATAAGCGGGCCG-TA	GTTCATAAGCGGGCG-TA	GTTCATAAGCGGGCG-TA	GTTCATAAGCGGGCG-TA	
	HCV-1	HCV-J	HC-J6	HC-J8	HD10-1-25	, HD10-1-3	BR36-20-164	≅ BR36-20-166	∯ BR36-20-165	SHFF	T (R	HCV-1	F-A.7	HC-J6	HC-J8	HD10-1-25	HD10-1-3	BR36-20-164	BR36-20-166	BR36-20-165	
• • •																					

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Figure 6 . Continued 6

5240 AAGGCCCTGGGCCTCCTGCAGACCGGGTCCCGTCAGGCAGG	5241 CCCTGCTGCTGCCAACTGGCAAAACTCGAGACCTTCTGGGCGAAGC T-C-TG-TG-TGGG-GC-TGT
HCV-1 HCV-J HC-J6 HC-J8 HD10-1-25 HD10-1-3 BR36-20-164 BR36-20-166 BR36-20-165	HCV-1 HC-J HC-J6 HC-J8 HD10-1-25 BD10-1-3 BR36-20-164 BR36-20-165

	1290 1300 1310 1320 1330 ITTGSPITYSTYGKFLADGGCSGGAYDIIICDECHSTDATSILGIG	1340 1350 1360 1370 1380 TVLDQAETAGARL.VVLATATPPGSVTVPHPNIEEVALSTTGEIPFYGKAI
	SEQ ID NO	
	1a 2a 2b 5a	1a 2a 2b 5a
Figure 7	HEATS STATE SHEET STATE SHEET STATE SHEET SALES	(BULE 26) HC1 HC18 HC18 BE-95

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Figure 7 - Continued 1 HCV-1 1a PLE HCV-1 1b -1v-1 HCV-1 Last HCV-1 Last HCV-1 Last HCV-1 Last HCV-1 Last HCV-1 Last HC-1 Last Last HC-1 Last Last Last Last HC-1 Last	nued 1	1390 1400 1410 1420 1430 bi evirgerehi techsikkindel AAKI: VALGINAVAYYRGLDVSVIPTSG	-I-A	SYQ-	AF	AFAAAQ-TSVAA-		1440 1450 1460 1470 1480	DVVVVATDALMTGYTGDFDSVIDCNTCVTQTVDFSLDPTFTIETITLPQD			\-0-L\A-S-I	CSFSAT-V
Figure F	- Conti	ç	<u> </u>	- 2a	З Р	5а			<u>a</u>	19	2a	Sb	5a
	Figure 7	1-11-11	HCV-J				te sh	IEÉT	INUI HCV-1	F 2	9F-3H	HC- J8	BE95

Figure 7 - Continued 2

				7	71/111							
1530	WYEL	:	:	:	-0-	1580	Kasg	Y	:	-9	G	-g
1520	LCECYDAGCA		A-	- Y		1570	HIDAHFLSQT				W	-
1510	RPSGMFDSSV		.AA-	-Λ	-ΛQ	1560	*WEGVFTGLTI	S			-5WN	DS
1490 1500 1510 1520 1530	SIYRFVAPGEF	·1	Y-ST	۰۰۲-۵۶-۳	Y-SA	1540 1550 1560 1570	LPVCQDHLE				-	۵
1490	AVSRTQRRGRTGRGKPG1YRFVAPGERPSGMFDSSVLCECYDAGCAWYEL	A	S	SAA	S	1540	TPAETTVRLRAYMNTPGLPVCQDHLEFWEGVFTGLTHIDAHFLSQTKQSG	-V		-9	I	
						_						
						SEQ ID NO						223
	<u>~</u>	9	2a	25	5a		,	1 9	2a	2 p	5 a	3а
	HCV-1	HCV-J	HC-J6	HC-18	BE95		HCV-1	HCV-J	HC- J6	HC-18	BE95	BR36
				0115	OTITI ITT	CHER	7 /0	w 11 F	00			

Figure 7 - Continued 3

1630	LYRLGA	!	S		۵	d		1680	STGCV	-TS-		I	-TV-S-	^-
1620	TLHGPIPL		\					1670	LAALAAYCI		·V	\\	Λ	
1610	WKCL IRLKF		1	T	M	\		1660	STWVLVGGV		A	AS-		T
1590 1600 1610 1620	AQAPPSWDQM		-KV-	-KV-	-KT-	E-		1640 1650 1660 1670	ICMSADLEVVT			0IM-		·-1
1590	ENLPYLVAYQATVCARAQAPPPSWDQMWKCLIRLKPTLHGPIPLLYRLGA		-FAT	FATKK	FT	L-FST-T		1640	VQNE I TLT HPVTKY I MTCMSADLE VVTSTWVL VGGVLAALAAYCLSTGCV	-STIN	-TVVAAAVA	AVAIMSAV	-S-^TIAII	II
	la E	lb D												
	-	_	ζ.	2	5a	3a			<u>a</u>	1b		8	Ω̈́	ñ
	HCV-1	HCV-J	HC-J6	HC-J8	BE95	BR36			HCV-1	HCV-J	HC-J6	HC-J8	BE95	BR36
							OUR	mm I	TE A	7110	FT /	D1 10	F 0	C)

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	1730	i	1 & ; လဲလက်က် ¹			
	1720	-5	SQHLPYIEGGMM LAEGFKG AS			
	1710	NS4-5		00	KH : : : : : : : : : : : : : : : : : : :	
			MEEC	1760	ETFWP	
	1700		VIVGRVV LSGKPAIIPDREULYREFDE MEECIIR-V	1750	ALGLLGTASRQA	
	1690	NS4-1	411PDREV -V VVAK VVAK-I	9 г	4 EVIAPA - AAV - QD-Q - QD-Q - QD-Q - TLK	
			LSGKP- R- VNGRA -NDRV	1740	atasra/ tk- -ak- -a-t -r-ta-c s-tgak	
4 <u>Jed</u>			VIVGRVV 111 C-ILH S-ILH HIE	NS4-7	ALGLL 10	
- Contin			1a 2a 2b 3a 5a		1a 1b 2a 2b 3a 5a	
Figure / - Continued 4			HCV-1 HCV-J HC-J8 HC-J8 BR36 BE95		HCV-1 HCV-J HC-J8 HC-J8 BR36 BE95	
1						

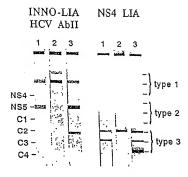


Figure 8

00	ATGAGCACGAATCCTAAACCTCAAAGAAAACCAAAAGAAACACCAACCG					51 100	TCGCCCACAGGACGTCAAGTTCCCGGGCGGTGGTCAGATCGTTGGCGGAG				
SEQ ID NO	64	51	41	43	23						
ซ	PC-3-4	E PC-3-8		∃ PC-2-6		ET Æ	FC-3-4	% PC-3-8	PC-2-1	PC-2-6	PC C/E1

Figure 9

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Figure 9 . Continued 1	101 TTTACTTGTTGCCGCGCGCGCCCTAGGATGGGTGTGCGCGCGC		151 AAGACTTCGGAACGGTCGCAACCCCGTGGACGCGTCAGCCTATTCCCAA	
Figure 9	PC-3-4	PC-2-1 PC-2-6 PC C/E1	PC-3-4 PC-3-8	PC-2-1 PC-2-6 PC C/E1

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CCCTTTACGCCAATGAGGGCCTCGGGTGGCCAGGGTGGCTGCTCCCCT GGCGCGCCAGCCCACGGGCCGGTCCTGGGGTCAACCCGGGTACCCTTGGC - Continued 2 251 201 Figure 9 PC-3-4 PC-3-8 PC-2-1 PC-2-6 PC C/E1 PC-3-4 PC-3-8 PC-2-1 PC-2-6 PC C/E1

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01 350	CGAGGCTCTCGGCCTAATTGGGGCCCCAATGACCCCCGGCGAAAATCGCG					_	351	TAATTTGGGTAAGGTCATCGATACCCTAACGTGCGGATTCGCCGATCTCA				
301			-	•	•		33		8	;	•	
	PC-3-4	PC-3-8	PC-2-1	PC-2-6	PC C/E1			PC-3-4	PC-3-8	PC-2-1	PC-2-6	1111

Figure 9

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	501 550
C-3-4	GAATTTACCCGGTTGCTCTTTCTCTTTATTCTTGCTCTTCTCGT
C-3-8	
c-2-1	1 1 1 1 1 1 1 1 1 1 1 1 1 1 1 1 1 1 1 1
C-2-6	
C-4-1	
C-4-6	
c c/E1	
	551
C-3-4	GTCTGACCGTTCCGGCCTCTGCAGTTCCCTACCGAAATGCCTCTGGGATT
2-3-8	
C-4-1	
9-4-2	
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Figure 9 - Continued 6	650 TATCATGTTACCAATGATTGCCCAAACTCTTCCATAGTCTATGAGGCAGA	700 TAACCTGATCCTACACGCACCTGGTTGCGTGCCTTGTGTCATGACAGGTA
Figure 9	PC-3-4 PC-3-8 PC-4-1 PC-4-6 PC C/E1	PC-3-4 PC-3-8 PC-4-1 PC-4-6

ATGT GAGT AGAT GCT GGGT CCAAAT TACCCCT ACACTGT CAGCCCCGAGC CTCGGAGCAGTCACGGCTCCTTCGGAGAGCCGTTGACTACCTAGCGG - Continued 7 701 751 Figure 9 PC-3-4 PC-3-8 PC-4-1 PC-4-6 PC-3-4 PC-3-8 PC-4-1 PC C/E1 PC-4-6

- Continued 8	850 AGGGGCTGCCCTCTGCTCCGCGTTATACGTAGGAGACGCGTGTGGGGCA	851 CTATTCTTGGTAGGCCAAATGTTCACCTATAGGCCTCGCCAGCACGCTACG
Figure 9	PC-3-4 PC-3-8 PC-4-1 PC-4-6 PC C/E1	PC-3-4 PC-3-8 PC-4-1

	901 GTGCAGAACTGCAACTGTTCCATTTACAGTGGCCATGTTACCGGCCACG										
,	GTGCAGAACT	1 1 1 1 1 1 1 1 1 1 1 1 1 1 1 1 1 1 1 1					951	GATGGCA			
	PC-3-4	PC-3-8	PC-4-1	PC-4-9	PC C/E1	SU	BSTI	를 PC-3-4	苗 PC-4-1	9-7-Jd (R	PC C/E1

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3890 ACCACTGGCAGCCCCATCACGTACTCCACCTAGGG	3891 CAAGTTCCTTGCCGACGGCTGCTCGGGGGGCCCTTATGACATAATAA CAAGTTCCTTGCCGACGGCTGCTCGGGGGGCCCTTATGACATAATAA ACTGCGAC	3941 ITTGTGACGAGTGCCACTCCACGGATGCCACATCCATCTTGGGCATCGGC	-AC
NO 1a 1b 2a 2b 2b 2b 5a 3a 3a	11 22 23 33 34 34 35 36 36 36 36 36 36 36 36 36 36 36 36 36	1a 1b	. 22 22 22 23 24 25 25 25 25 25 25 25 25 25 25 25 25 25
SEQ ID 197 199 222			
HCV - 1 HCV - J HC - J6 HC - J8 PC1 37 C1 48 BR36	NAME OF THE PROPERTY OF THE PR	E 26)	HC-J8 PC1_37 PC1_48 BR36

4040 ACTGTCCTTGACCAGGGAGGGGGGGGGGGAGTTGTGCTCGC -A	4041 CACGCCACCCTCCGGGGTCCGTCACTGTGCCCCATCCCAACATCGAGG	4091 AGGTTGCTCTGTCCACCGGAGAGATCCCTTTTTACGGCAAGGCTATC -AG-CATTCTACG-CGGGCAGAGG-TTTTG-CTGGGCAGAGG-T
11 1 1 1 1 1 1 1 1 1 1 1 1 1 1 1 1 1 1		12 12 23 52 53 33
HCV-1 HCV-J HC-J6 HC-J8 PC1 37 PC1 48	MAN STATE OF THE COLUMN THE COLUM	102 TE 20) HCV - 1 HCV - 1 HC - 16 HC - 18 PC1 - 37 BR36

4141 CCCCTCGAAGTAATCAAGGGGGGAAGACATCTCATCTTCTGTCATTCAAAA-T-G-CC	4240 GAAGAGGCAAAGCTGGCGCAAAGCTGGTTTGGGCATCAATG
112 122 123 133 133 133	11 32 2 2 2 2 2 2 2 2 2 2 2 2 2 2 2 2 2
HCV-1 HCV-J HC-J6 HC-J8 PC1_37 PC1_48 BR36	HC-18

4291 GATGTTGTCGTCGCAACCGATGCCTCATGACCGGCTATACCGGCGACCTACTAGTTCAGCCC	4341 CTTGGACTCGGTGATAGACTGCAATACGTGTGTCACCCAGACAGTCGATT	4391 TCAGCCTTGACCCTACCTTCACCATTGAGACAATCACGCTCCCCCAGGATT-GTG-CAG-CAACT-GTC-ACAGTTGTTG
112 22 2 2 2 2 2 2 2 2 2 2 2 2 2 2 2 2	11 12 22 23 23 23 23 23 24 25 25 25 25 25 25 25 25 25 25 25 25 25	110 210 220 52 33
HCV-1 HCV-J HC-J6 HC-J8 PC1_37 PC1_48	HCV-1 HCV-U HCV-U HCV-U HC-U8 HC-U8 PC-18 PC-14 BR36	(95 370) (97 37) (97 37) (97 37)

4441 CONGRESS & CONGRESS & CONGRE	GGGTG-GGGGAT	AT-GCGCC-C-GA-GA-TG		AGA-A-GCGTC-CGGAT-GAC	AGA-A-GCGAC-CGGAT-GAC		4491	CATCTACAGATTTGTGGCACCGGGGGGGCGCCCCTCCGGCATGTTCGACT		TTTG-ATT-CA-TTAGAAAA	-G-TG-ATT-GT-ACA-GGTGA	AC-G-ACT-GG-TAA-AGT	AC-G-ACT-GG-TAA-NT-A		4551	CGICCGICCICIGIGAGIGCIAIGACGCAGGCIGIGCIIGGGIAIGAGCIC	ggg	GTGTAGCCTGGCCA	GCGTAGCTCGGCACT	-CGTGG	-CGTGGTCTCAGTG	
6	1 1	2a	2b	รล	5а	3a		1a	1p	2a	2b	ъ	3.52 3.02 3.03			18	1p	2а	2 b	Бa	5а	3а
HOW.	HCV-J	HC-76	HC-J8	PC1 37	PC1_48	BR36	SU	LSH HCV-1	UHCV-√	HC-J6	HC-J8	H PC1 37	3) PC1 48	26)		HCV-1	HCV-J	HC-J6	HC-J8	PC1 37	PC1 48	BR36

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4641 a GCTTCCGTGTGCCAGGACCATCTTGAATTTTGGGAGGCGTCTTTACAG TG	1a GCCTCACTCATATAGATGCCCACTTTCTATCCCAGACAAAGCAGAGTGGG 1bCG
HCV-1 HCV-J HC-J6 HC-J8 PC1 37 PC1 48	1CV - 1 1CV - J 1C - J 6 1C - J 8 1C - J 8 2CI - J 8 3R3 6
	4641 a GCTTCCGTGTGCCAGGACCATCTTGAATTTTGGGAGGGCGTCTTTACA 1b TT-GC

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4741	GAGAACCTTCCTTACCTGGTAGCGTACCAAGCCACCGTGTGCGCTAGGGC	CGG	ATT-CG-AT-AACCGTA	ATG-GTAACGCGAAC	T-T-CAT	TT-NATAACT-T-C-C-	CTCT-CT-G-TACTCTC-C	701	TCAAGCCCCTCCCCATCGTGGGACCAGATGTGGAAAGTGTTTTTATTTTCCC	GTATA	CA	AA-GTTGTC-A-C-A-G-	GAGCCAGCACAACACA	GAGCCAGCACAACAC	GGTAGTG	1707		1-AAGUUGACUTUUATIGGGUUAACACCCCTGCTATACAGACTGGGCGCT	-AAGGGGGG		ATAGACTCCGCG-	AGNT-AACCTTCT-GG	AGTI-AACC-TICI-GG	-TAAAATGTTTC-GTGC
	la	1b	2a	2b	Бa	5а	3a		19	1p	2a	2b	5a	<u>5</u> а	3a		(d T	1p	2a	2p	5a	<u>5</u> а	3a
	HCV-1	HCV-J	HC-J6	HC-J8	PC1 37	PC1_48	BR36		HCV-1	S HCV-J	SS HC-16	HC-JB	37 FC1 37	# PC1 48	H BR36	(RUI	E	7 26	FCV-J	HC-J6	HC-J8	PC1 37	PC1_48	BR36

4891 GITCAGAATGAAATCACCCTGACGCACCCAGTCACCAAATACATCATGAC			CAG- 4941	ATGCATCGGCCGACCTGGAGGTCGTCACGAGCACCTGGGGTGCTCGTT	CCAATAAAAAAAAA			4991 5040	GCGGCGTCCTGGCTGCTTTGGCCGCGTATTGCCTGTCAACAGGCTGCGTG				-GTGGCCGCTA-GGTGT-CGA	-GTGGCGCTA-GGTGT-CGA	$-\mathtt{A} - \mathtt{G} - \mathtt{C} -$
1. 1.a	23 23 25	n m	В	13 13	Ib 2a	2b	, n n n	ช า	19	1p	2a	2p	5a	Sa	3a
HCV-1	HC-48	PC1_37 PC1_48	BR36	HCV-1	HCV-J HC-J6	HC-J8	PC1_37 PC1_48		HCV-1	HCV-J	HC-J6	HC-JB	PC1_37	PC1_48	BR36

5041	GTCATAGTGGGCAGGGTCGTCTTGTCCGGGAAGCCGGCAATCATACCTGA	TTAA	TGCA-CC-CT-GCA-G-TAA-CA-CGAG-C-TCG-TGCG	TCCA-TC-CC-ACA-CAAT-ATCG-GTTTG-GGCCC	-CCTAAC-CTATCTC	-CCTAAC-CTATCTC	GTTCATAAGCGGGCG-TA	5140	CAGGGAAGTCCTCTACCGAGAGTTCGATGAGATGGAAGAGTGCTCTCAGC	TGICA-	AGTGAG-CTTGATG-CTCTA	AAT-ATGAG-CCTAG-CTCCA	TGAT-AAGC-AT	TG-CAT-AAGC-ATGGGCCT	AAGGT-GT-A-C-A-AAG	5141	ACTTACCGTACATCGAGCAAGGGATGATGCTCGCCGAGCAGTTCAAGCAG	C-CTAACA	GAGCGG-TCTTAG-GCA-CG-A-AAT-C-GTCC	-AGCCG-CCTTGCA-CG-A-GGAT-CATCT	CGGCTGCGACACGTGCCA-TGAAAG	CGGCTGCG-GACACGTGCCA-TGAAAG	CTGCCATACTCA-G-AA-ATC-CG-A
	1,8	1p	2a	2b	5a	5а	3a	-	1a	1p	2a	2b	5 a	5a	3,8		1a	1p	2a	2b	5a	5 a	3a
	HCV-1	HCV-J	HC-J6	HC-J8	PC1 37	PC1_48	BR36	SUE	ISS HCV-1	IL HCV-J	HC-J6	## HC-J8	FC1 37	DA PCI 48	BK36		HCV-1	HCV-J	HC-J6	HC-78	PC1 37	PC1_48	BR36

rigare to - continued y	5191 5240 1a baggddonnagaddnagagaddagaddandagadaanaanaa	11	2a	2b	Sa	5a	3a	5241	1a CCCTGCTGTCCAGACCAACTGGCAAAACTCGAGACCTTCTGGGCGAAG	1b	2a	2b	വ	57a	3а	200	·			2a C				3a
- of ainstr	HCV-1	HCV-J	HC-J6	HC-J8	PC1 37	PC1_48	BR36		HCV-1	III HCV-J	<u>⊆</u> нс-л6	8D-78	而 PC1 37	DC1_48	171 BR36	E 26)	HCV-1	HCV-J	HC-J6	HC-J8	PC1 37	PC1_48	BR36

	SEQ ID NO 56 58	
<u>e 11</u>	1286 HCV-1 TTGSPITYSTYGKFLADGGCSGGAYDIIICDECHSTDATSILGIGTVLDQAETAGARLVV HCV-JG	1346 ATATPGSVTVPHPNIEEVALSTTGEIPFYGKAIPLEVIKGGRHLIFCHSKKKCDELAA ATATPGSVTVPHPNIEEVALSTTGEIPFYGKAIPLEVIKGGRHLIFCHSKKKCDELAA ACUJU
Figure 11	HCV-1 HCV-J HC-J6 HC-J8 PC-1-7	MACOUNT THE COLOR OF THE COLOR

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DFDSVIDCNTCV	A
HCV-1 HCV-1	HC-78

26)

1586 LVAYQATVCARAQAPPSWDQMWKCLIRLKPTLHGPTPLLYRLGAVQNBITLTHPVTKYI	$ \begin{array}{cccccccccccccccccccccccccccccccccccc$	1646 HCV-1 MTCMSADLEVVTSTWVLVGGVLAALAAYCLSTGCVVIVGRVVLSGKPALIPDREVLYREF HCV-0 A	1706 HCV-1 DEMEDCSQHLPYIEQGMMLAEQFKQKALGLLQTASRQAEVIAPAVQTNWQKLETFWAKH HCV-0
HCV-1 HCV-J	HC-J6 HC-J8	HCV - 1 HCV - J HCV - J HC - J6 HC - J6 HC - J6 HC - J7	HCV - 1 HCV - 1 HC - 76 HC - 76 HC - 16 HC - 18 PC - 1 - 48

330 340 370 370 370 370 370 371	380 390 400 410 420 E2	A
330 340 35 	380 390 4C 4C 5-6-6-6-6-6-6-6-6-6-6-6-6-6-6-6-6-6-6-6	A
10 12 25 33 35 35 35 35 35 35 35 35 35 35 35 35	τυ <u>τ</u>	22 28 38 38 38 58 9
HCV1 HCVJ HCJ6 HCJ8 NZL1	H 695	HCVJ HCJ6 HCJ8 NZL1 HCVTR BE95

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GWGPISY AN	MG HT	AI 0-FD-	TLE-ET-	CTJ	1	1		520		VGTTDRSGAP			K0-N-	-		-H-78
SCRPLTDFDG	IDE-A-	ASIFA-RV	G-DRI	K-I-F-R-	:	A-A		510		VYCFTPSPVV						i
FNSSGCPERLA	-AM-	SW	S	TS		-M-Q	i	200	•	IVPAKSVCGP	S0	V-S-S	RI	S	ı	IS-DKRV@F
<i>«</i> LAGLFYHHKF	FI-AA-R-	-S1-S	LS	λI ₌		λI:	į	490		CWHYPPKPCG	A-R	RQ	R	A-RD		R
NCNDSLNTG	0	H	0	E-I		0	;	480		GSGP/DQRP)	PESS/	VTN-E-M	VTNDG-M	ITS-D		IS-DK
ĵa	1	2a	Sb	3a	3b	Sа				1a	1 b	2a	Sb	3a	3b	5a
HCV1	HCVJ	HCJ6	HCJ8	NZL1	HCVTR	BE95				HCV1	HCVJ	HCJ6	HCJ8	NZL1	HCVTR	BE95
	1a	6 6	1a 1b 2a	1a 1b 2a 2b	. 1a 1b 1a 2b 3a	1a 1b 2a 3a 3b	 1a 1b 2a 3a 3b 5a	. 22 23 33 34 58 58		2 2 2 2 3 3 3 5 3 5 3 5 3 5 5 8 5 5 8 5 5 8 5 5 8 5 5 8 5 5 6 5 6	2 2 2 2 2 2 2 2 3 2 2 3 2 3 2 3 3 3 3 3					

-----E---LL--TRP-QG *LYSWGENDTDVFVLNNTRPPL* --N--S-V--F-LM----540 * 530 Figure 12 · Continued 2 1a 1b 3a 3a 3a 5a HCV1 HCVJ HCJ6 HCJ8 NZL1 HCVTR

101/111 5																							
086	CCCCTACGACGGCGTTGGTAATGGCTCAGCTGCTCCGGATCCCACAAGCC	G-AGG-AAA		-AACC-AGG-AT-GA	-GCAACC-AGGT-GT-A	-AAACC-AGGT-GT	-AAACC-AGGT-GTT	-GAACC-AGGT-GT-AT	-GAACC-AGGT-GT-AT	-GAATC-AGGT-GT-AT	-GACAGGT-GTT	-AAACAGGT-GT-A	-GAACC-AGG-AT-GAT	-AAACC-CGI-GII-A	-GCG-TA-CAA-CCGT-CGC-A-GCGCG-G-T-	-TATCTTA-CAA-CC-CCT-CGCCGCTTG-TCGCTG	-ACG-CA-CAA-CCGT-CGC-A-GCGCG-G-TT	-AATCTTA-CAA-CC-CCT-TGCCGCTTG-TTG-GCTA	CG-TGTGTAGGGTG-CGTT-ACGA	CG-TGTGTAGGGCG-CGTT-GCGA	CG-CGTGTAGG-AGTG-CGTT-GCGA	CG-CGTGTAGGGCG-TGTC-GCGA	-AATCC-GGCT-AGTCTG
	Ιa	1a	1a	1p	1p	1p	1p	1p	1p	110	1p	1b	1p	1p	2a	2b	2a	2p.	3a	3a	3a	3a	5a
SEO ID																							157
	HCV-1	HCH-H	HC-J1	HCV-J	HCV-BK	HC-J4.83	HC-J4.91	HCV-JTA	HCV-JIB	HCV-CHINA	HCV-T	HCV-JK1	HCUNK	HCV-N	HC-J6			HC-J7	NZL1	HEM26	TH85	US114	BE95
								SU	RS	Π	JIE	SH	itt	ı (t	IUL	E 21	3)						

1030	ATCTTGGACATGATCGCTGGTGCTCACTGGGGAGTCCTGGCGGGCATAGC	AAA		GGG-G-GGGCTAC-T	GGG-G-G-G-G-C	GGG-GGGGGGGGG	GG	GGTG-GGGC	GGTG-GGGC	GA	GGTG-GGGC		A	GA-CG-GGGC	A-ACT-GCGTCATTCT	GC-CATTTTCC-GCTTGGTTTT-G-	- 1	GC-IGG-IGIICC-GCICGGIIII-G	T-GCAGCGC-TCAT	T-GCAACGCTCATC	T-GCAACGCTCATC	T-GCTAG-ACGCTCATC	GA-TCAGAGCGTTTT-C-GCC
	la	1a	T B	1p	1p	1p	1p	1p	1p	1p	1p	1p	15	1p	2a	2p	2a	2b	3a	39	39	39	S B
	HCV-1	HCH-H	HC-J1	HCV-J	HCV-BK	HC-J4.83	HC-J4.91						_	HCV-N	111			HC-J7	NZL1	HEM26	TH85	US114	BE95

-I-I-
ICCIA-CGC-GCII-I
A-C
AC-ATG-ATCCTA-C
AC-
Бa
BE95

1130	TATTTGCCGGCGTCGACGCGGAAACCCACGTCACCGGGGGAAGTGCCGG		-GCAAATTCAAC	-CTTG-C-C	-TTTGTGTGATT-	-CC	1	-CGTCGCAA-CT	-CGTCGCAA-CT	-CCTT-GTTTT	-T	-CG-ACTTG-A	-C	-TGCACLER -TG-C-CT-ACAGGCACLER -	-GGCCGGCTAC-GTTTTC-A	-TGGAGTAACCT-TTCGCCAGGAAGT	-GGCCTAGTA-CG-AC-GTT-CTTCT	-TG-CAGTAGCATCTADAG-	-GCI-AGICC-CAI-IAC	-GT-AGTCAT-TACTCTC-	-GT-AGT-CGA-G-ATCB	-GT-AGTCAGCATATCTC-ATG-CT	-GAGTTACTGA-TT-GCCTCCAGC-
	Га	٦	1a	1b	1p	1p	1p	1 p	1 p	1 p	1p	1 p	1p	1p	2a	2b	2a	Sp	3 3	3a	3а	3а	5а
	HCV-1	HCH-H	HC-J1	HCV-J	HCV-BK	HC-J4.83	S HC-J4.91	SHCV-JTA	11	1	S HCV-T	HCV-JK1	HCUNK	N- N-N	9C-DH 2	9 HC-J8	HC-J5	HC-J7	NZL1	HEM26	TH85	US114	BE95

Figure 13 - Continued 5

1230 CGTCCAGCTGATCAACACCAACGGCAGTTGGCACCTCAATAGCAACAC	-AAAA	-AAA	AAACG-GACGCT-	A	1	A	AA	AACATCACG	GATATTCTACG	AATATTTT	AAATG-T	-CCGGC	AATATT	AACCTTA	-CT-TT-ATCA-ACC-GT	-C-TCTTCACC	TBTC	AC-GGTTCGA	AC-GGTTCGACT	-C-GTGTTCGAA	- 1	AC-GCATACACGC
1a	1a	Тa	1b	1 p	1b	1b	1p	1b	1p	1b	1b	1b	1b	2a	2p	2a	2p	3а	3a	3а	3а	S B
HCV-1	HCH-H	HC-J1	HCV-J	HCV-BK	HC-J4.83	HC-J4.91			HCV-CHINA			H HCUNK	HCV-N				HC-J7	NZL1	HEM26	TH85	US114	BE95

1280	TGAACTGCAATGATAGCCTCAACACCGGCTGGTTGGCAGGGCTTTTTTA		TA	TG-TCA-TT-C-		-ACTCTG-TCC-TC	DLD	G-TCIC-UV	ATCG-TCTG-TC	CTCTTG-LTC-IC	-AG-CTCC-G-TTC-TG-TTC-TCTCG	TCGTC-ATG-TCTC-C-C	J	JJ-5D-DI-D-IB-DCID	GICIL-GCLCC-C-GICAG	-CT	T	-CT	-ATGTC-A-AG-TTA-ATT-GT-		TAT-G-TCA-AG-TCA-ATAT-G-T	GTC-A-AG-TCA-ATT-G-T	-TTTCC-GTG-TCA-ACCCC
	1a	1a	1a	1p	1p	1b	1b	1b	1b	1b	1b	1p	1p	1p	2a	Sp	2a	3p	39	3а	3a	39	5a
	HCV-1	HCH-H	HC-J1	HCV-J	HCV-BK	HC-J4.83	HC-J4.91		SE HCV-JTB	HCV-CHINA			E HCUNK		THC-J6			HC-J7	NZL1	HEM26	TH85	US114	BE95

1330	CACCACAAGTTCAAGCTCTTCAGGCTGTCCTGAGAGGCTAGCCAGCTGCCG		AA	GCAGG-G-CCGCAC-CA-GT	ACAT-GT	ACAGGC-GC-G	ACA	GCA	GCA	ACAGG-G-CACG-AC-CA-G	GCGGG-GCGCAC-CA-G	GTAA-G	A-ATGG-GG-GCGCGC-CT-GCG-	ACATG	ACGCGA	ACAGCTCCC-CT-GT-TTC	GT-ACGCTGACC-TC-CGTGT	GT-AGACGTAGCTCCC-CT-GT-TTC	TT	T-TTTA-TA-TAC-CCAGTAA	TT	T-TA-TTA-TAC-ACAGTAA	TTTACGTCA-GTTA-	
	Тa	Тa	1a	1b	19	1p	1p	1b	1p	1b	1p	1p	1p	1p	2a	2b	2a	2р	3a	3a	3а	3a	5a	
	HCV-1	HCH-H	HC-J1	HCV-J	HCV-BK	HC-J4.83	HC-J4.91											HC-J7	NZL1	HEM26	TH85	US114	BE95	
								SI	BS	TITL	JΤΕ	SH	EE	(R	UL	E 21	6)							

400th	1		-AT-	TG	A-TG	A-TG	AG	AG	A-TG	A-TG	IG	A-TG	TG	3-A	4A	3-AT-	3A	-E	- L	-AA-	-I	1111
TATTOACTERIORS			DC	TCT-C				ATCCC		D	I G GGG	TCC	DD	G-CT-ACAAGAG	AA-CT-GGAACGAAA	A-CT-GCAACGAG	AA-CT-GGAAGAG	CT-A-CAG	T-CT-G-CAG	CT-G-CAG	T-CT-G-CAG	AAC
1380 ACCCTTACCGATTTTGACCAGGCTGGGGCTCCTATCAGTTAT			CA-CGATGC-CTGTCC-C-	CAAGA-A-GCATCT-C	CAGA-TGGC-CA	CAGAGGC-CA		CTAGA-A-GC-CTA	CAGATACACT	TTAGA-A-GCTATCCC	TAGA-AGGC-CTAG	CAGATACAC-CGG	CTAGA-A-GCA	CAGIA-CGAG-CCCGGGIAG-CT-ACAAGAG-A	CGGGGGACG-ATC	CAG-A-CGAG-CCCGGATAGA-CT-GCAACGAG-AT-	TAAGGGATCG-ATCGAA-CT-GGAAGAGA	GA-CTTTCCAGGA	GA-CTTCCCAGGG	GA-CTCCCA-TG	GA-CTTCCCAGGG	GGGAC
ď	L R	19	1p	1p	1p	1p	1 p	1b	1p	1p	1p	1 9	1 9	2a	2p	2a	2b	39	39	39	3a	5a
HCV-1	HCH-H	HC-J1	HCV-J	HCV-BK	HC-J4.83	HC-J4.91				ILCV-T		HE HCOINK		_			HC-J7	NZL1	HEM26	· TH85	US114	BE95

BACCAGCGCCCTACTGGTGGCACTACCCCCCA	ATT	A-GATG-GT	A-GATT	-TA-GTTTG-GT	TA-GTTTG-G-T		TA-GTTG-AT	1 1 1 1 1 1 1	1			A-GTT	A-AGTA	A-GGTG	A-AATA	A-AGTTG			AAAAT	AAAGT	AAAATT
GACCAGCGCCC	A	1 1 1 1 1		L	L	L	L	1	1	A	L	1	AGTAT-	3GAT-	AATAT	AGAT-	CTTG-C	CCAG-C	CTTG-C	CTTG-C	3TTG-C
1430 ACGGAAGCGGCCCC	1 1 1 1 1 1 1 1 1 1 1 1 1 1 1 1 1 1 1 1	TGCCTGAGAT-G	-GTCTA-AT-A	-GCCTGA-AG	-GCCT-A-AG	-GCCTG-ATG	-GCCTG-G-A-TTG	-GCCTGATAT-G	-G-CTGA-ATAG	-GTCTCAT-G	-GCCTCAT-ATTTG	-TCCT-AA-AG	-T-TC-C-AATAGAGTAT-A-AGT	TC-C-AA-GATGO	-T-TC-C-AATAG	-T-TT-C-AA-GAGGAGAT-A-AG	ATC-CTTTC	ATCTCTT-GTC	ATC-CTTC	ATC-CATT-TTCTTG-CAAAG	AT-TCGTAGTTG-CAAAAT
ю Н -	ນ ແ H ⊢	1b	1b	1b	1b	1b	1b	1b	1b	1b	1b	1b	2a	2b	2a	2b	3а	3а	3a	3a	5a
HCV-1	HC-J1	HCV-J	HCV-BK	HC-J4.83	HC-J4.91	HCV-JTA	HCV-JIB	HCV-CHINA	HCV-T	HCV-JK1	HCUNK	HCV-N	HC-J6	HC-J8	HC-J5	HC-J7	NZL1	HEM26	TH85	US114	BE95

110/111

1480	AAACCTTGCGGTATTGTGCCCGCGAAGAGTGTG	-GTCAC		CGGGCTC-CAG	CCCATT	CAT(-CATC-	-CATTC-	TC-	-CATTC-	CATC-		CGTATT-CAG	CAGTCA-ACG-TCCGAG-C-	-GAGTG-ACTGCTC	-GG	TCACG-T	GCCCI-GICGC	-GT-ACCGATCAC	-GTACCGCAATCAC	-GTAAA-GCAATCAC	-G-TT-ACCCGATCAC	CGGGAG-GACC-AGAGC
	1a	Тa	Тa	1p	1p	1p	1p	1p	1p	1p	1p	1p	1p	1p	2a	Sp	2a	Sb	За	3,8	3a	3a	59
	HCV-1	HCH-H	HC-J1	HCV-J	HCV-BK	HC-J4.83	HC-J4.91	S HCV-JIA	M HCV-JIB	HCV-CHINA	III HCV-T	S HCV-JK1	HCUNK	14	MC-J6		(9) HC-J5	HC-J7	NZL1	HEM26	TH85	US114	1 E